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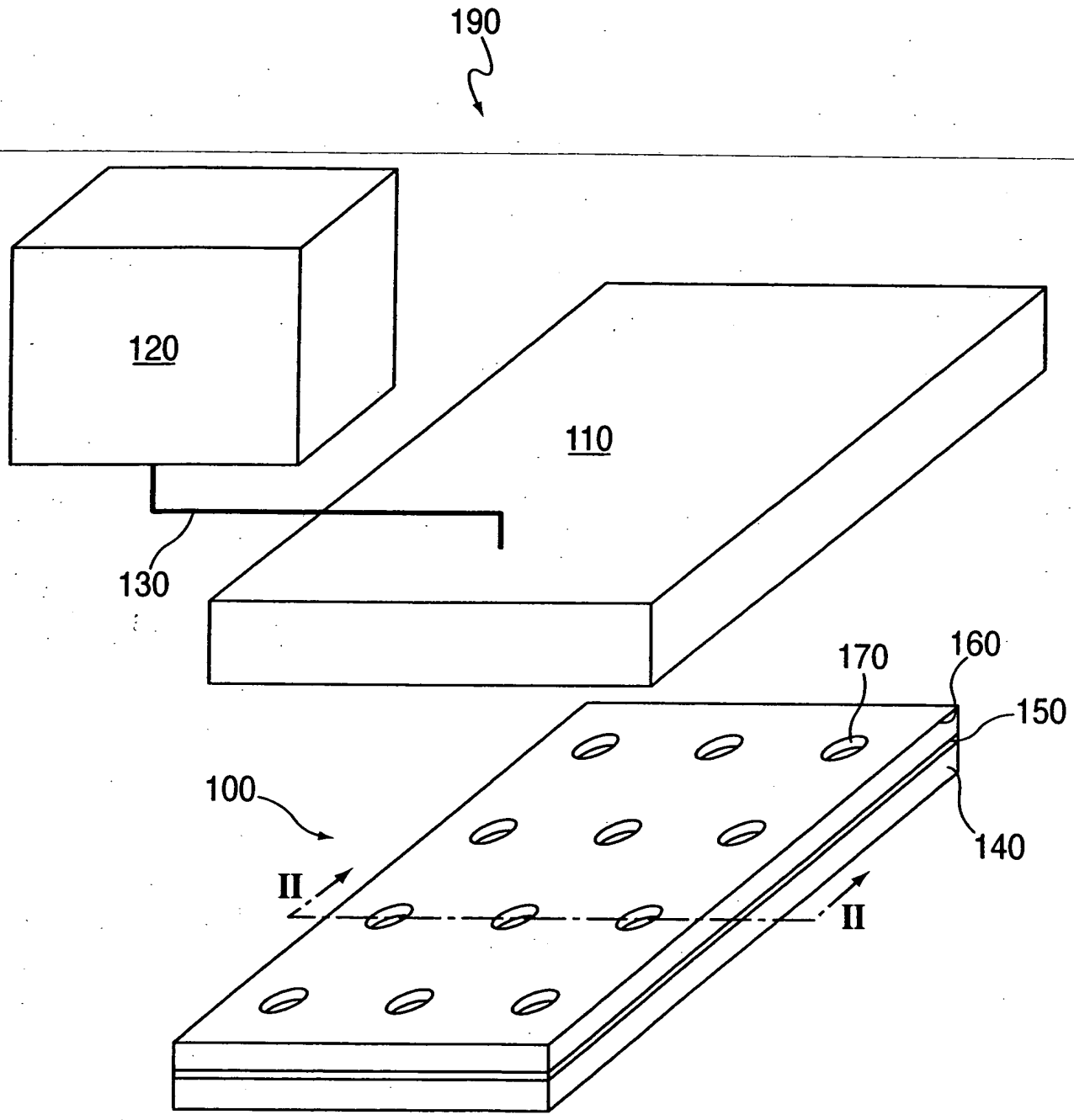


FIG. 1a

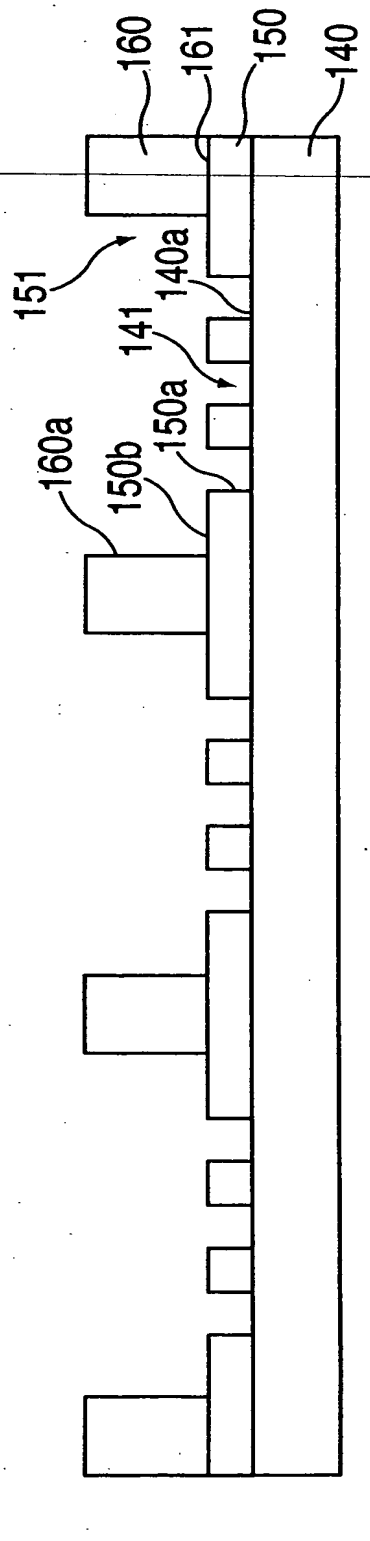


FIG. 1b

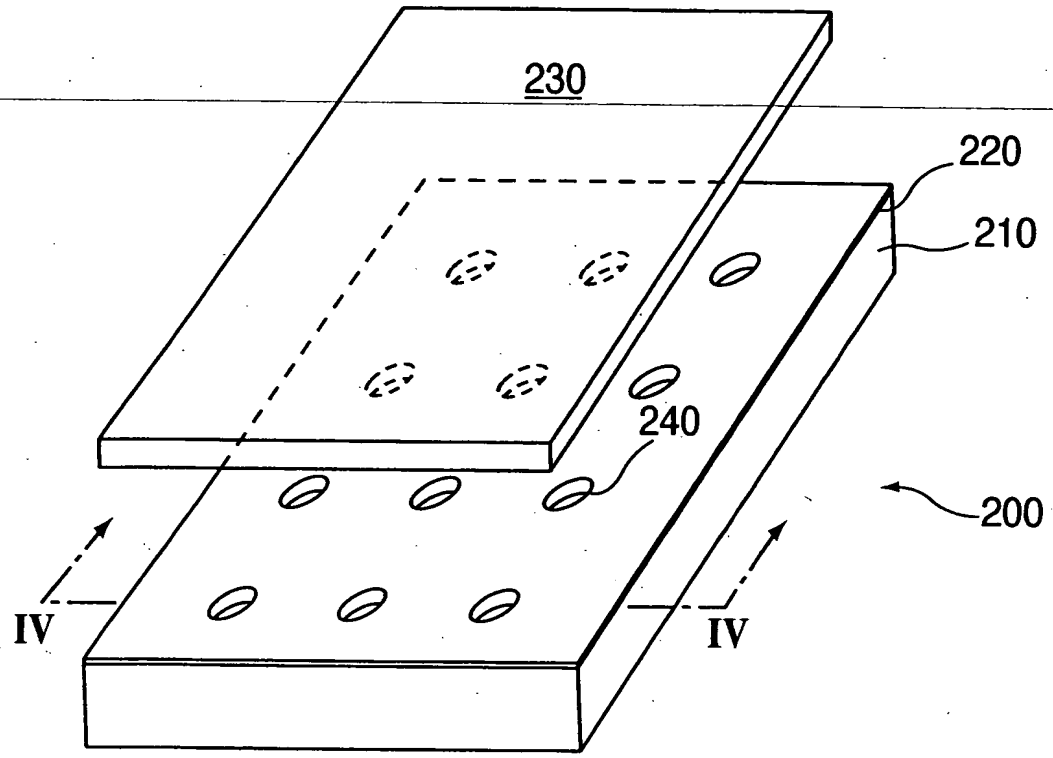


FIG. 2a

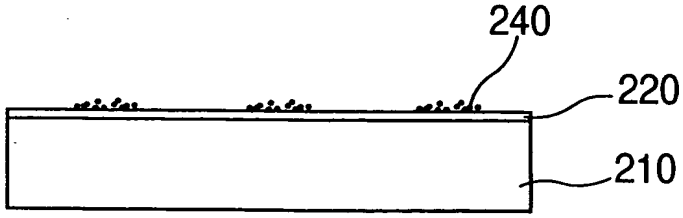


FIG. 2b

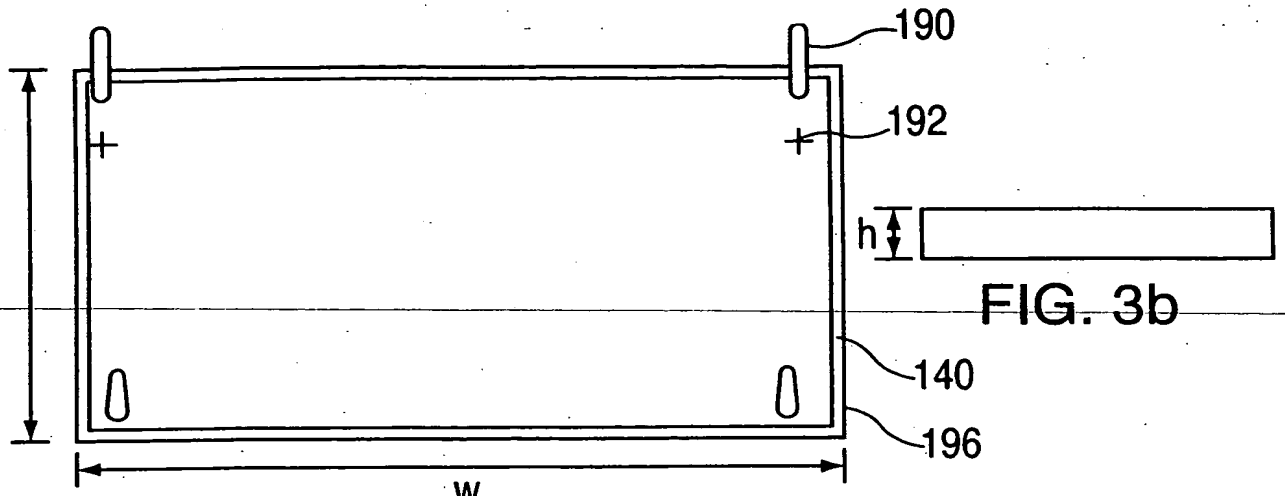


FIG. 3b

FIG. 3a

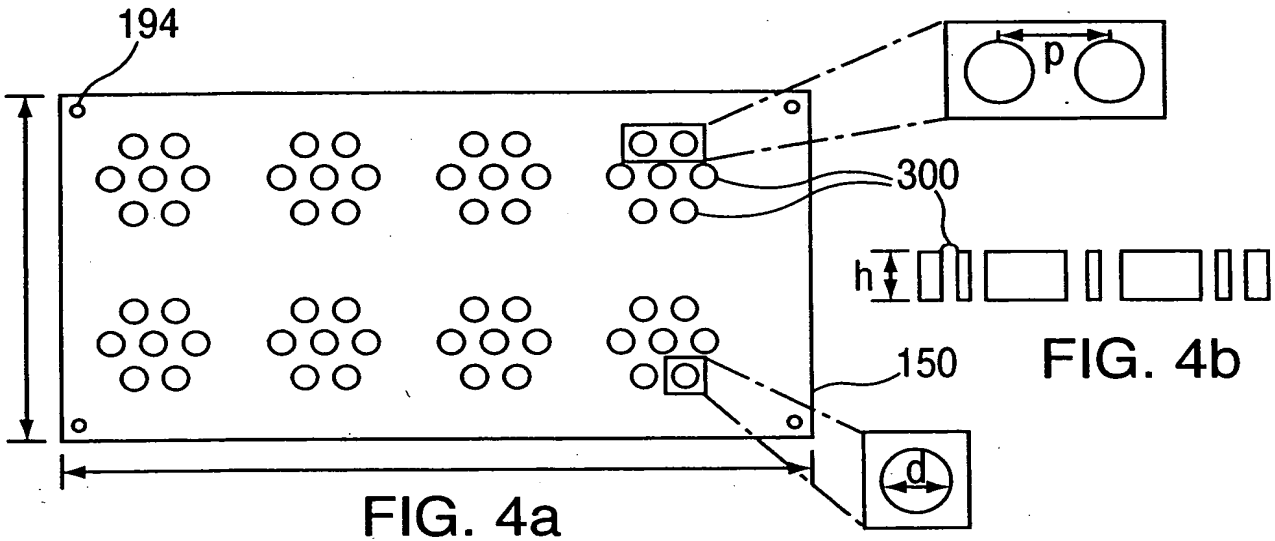


FIG. 4b

FIG. 4a

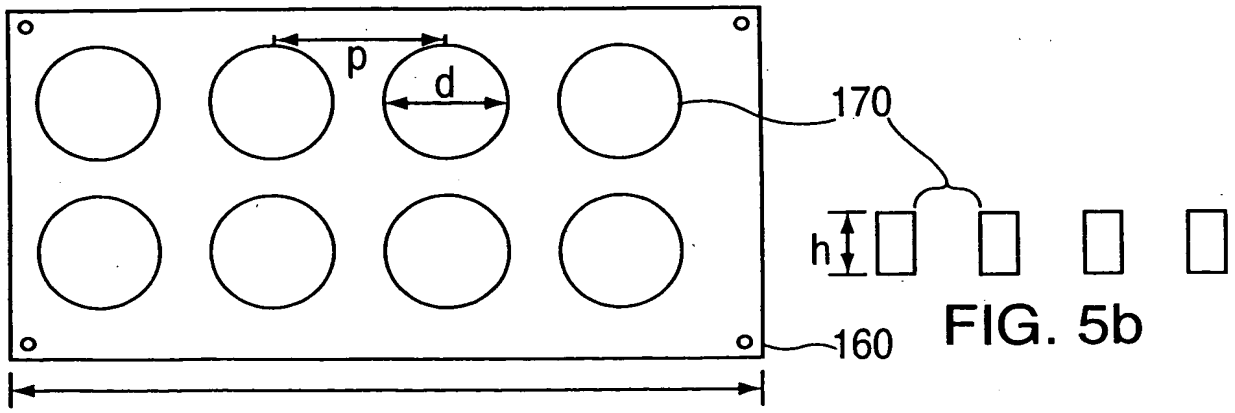


FIG. 5b

FIG. 5a

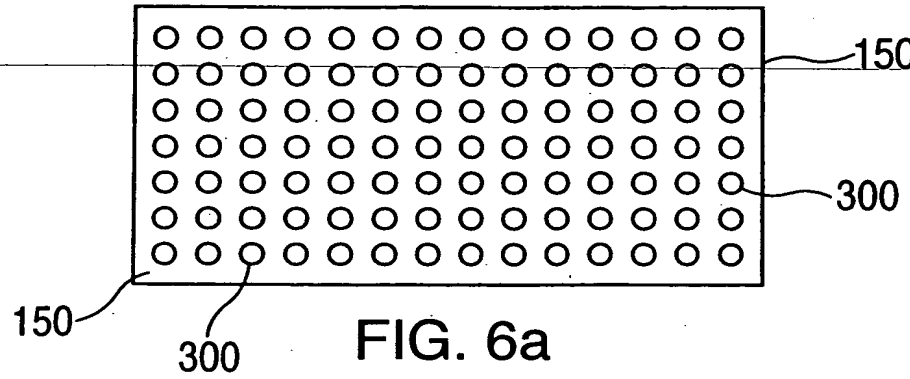


FIG. 6a

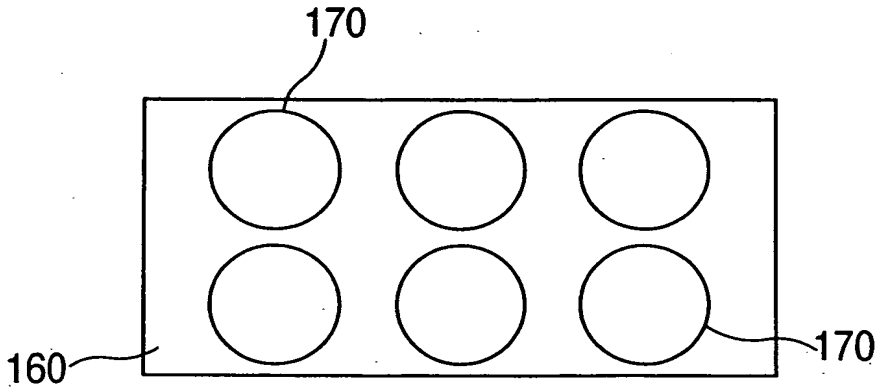


FIG. 6b

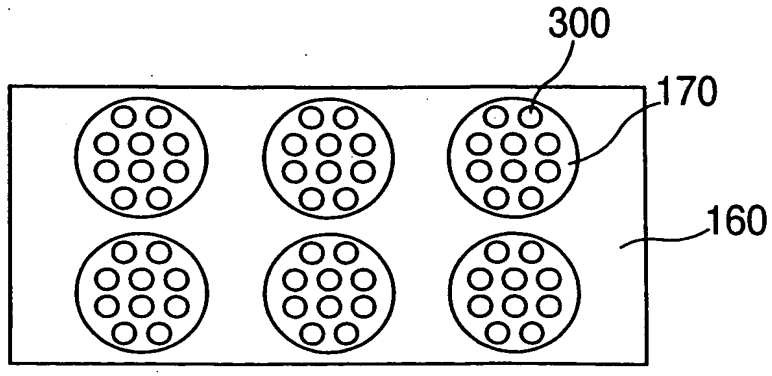


FIG. 6c

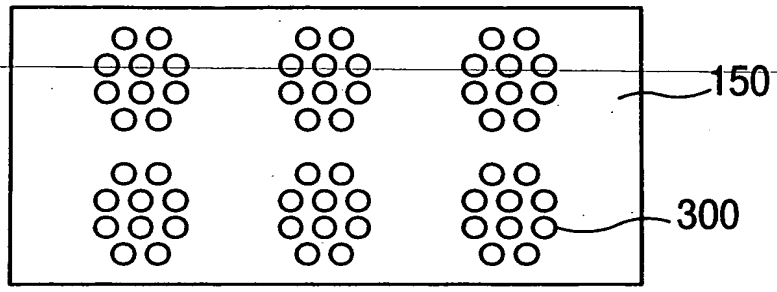


FIG. 7a

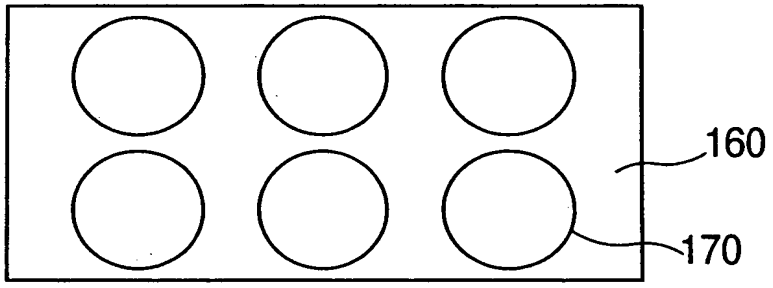


FIG. 7b

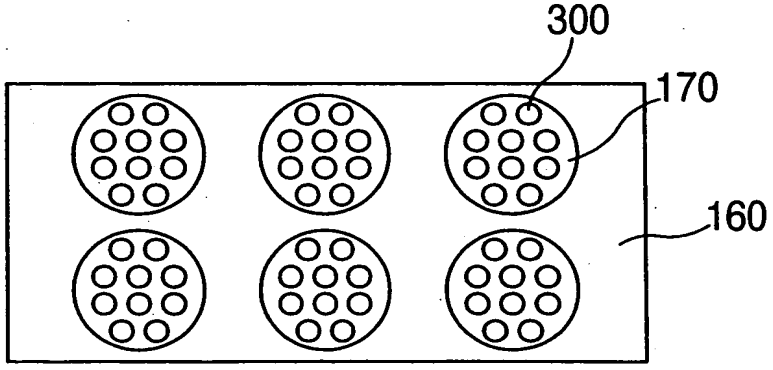


FIG. 7c

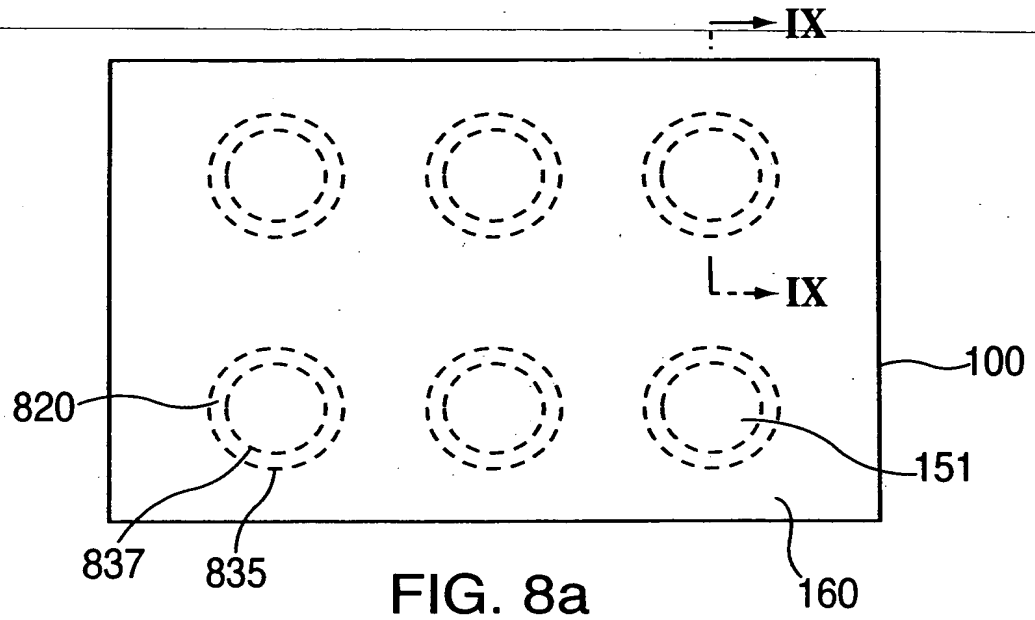


FIG. 8a

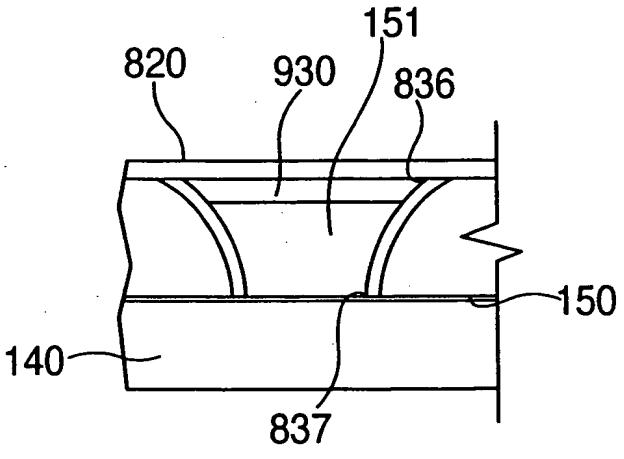


FIG. 8b

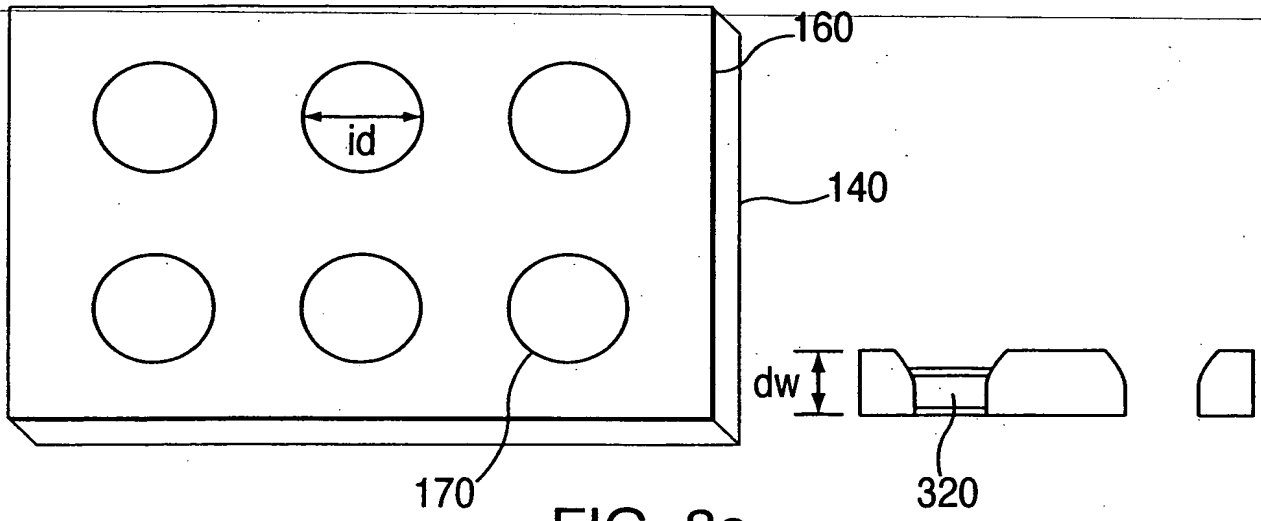


FIG. 8c

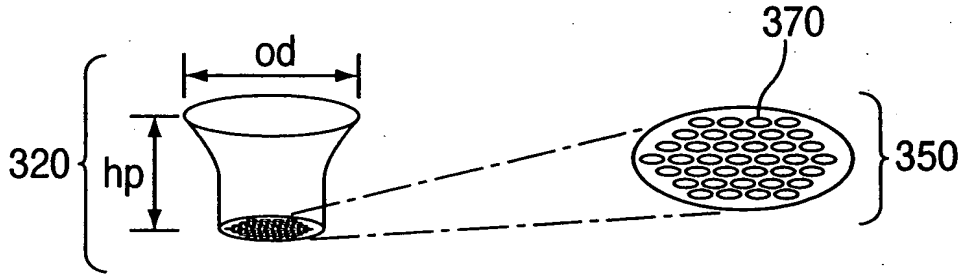


FIG. 8d

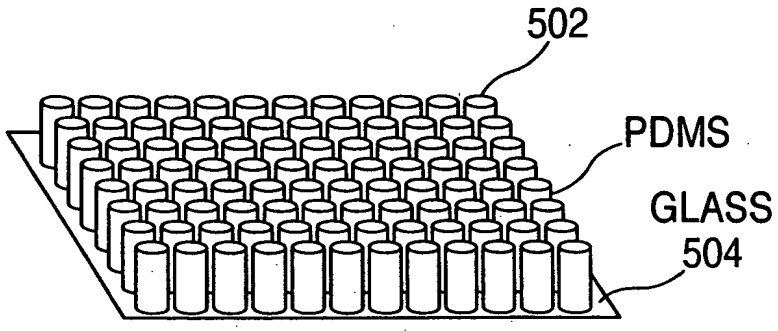


FIG. 9a

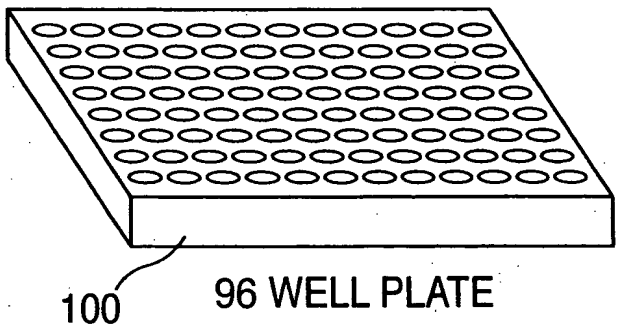
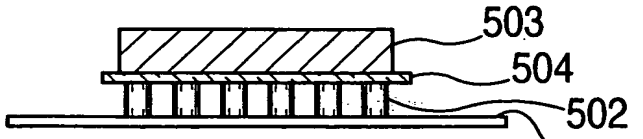


FIG. 9b



1) PLACE PDMS MACROPOSTS

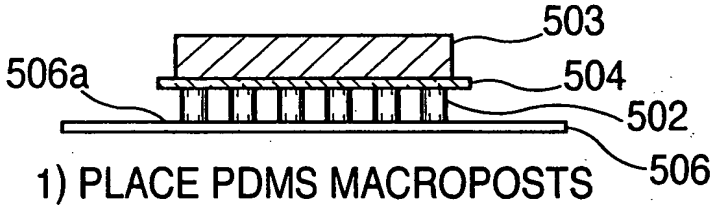
FIG. 10a

2) POUR PDMS

FIG. 10b

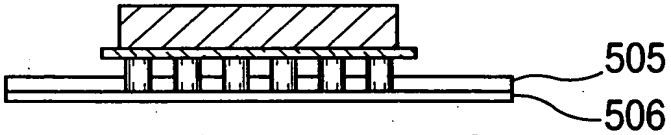
3) CURE AND REMOVE MACROPOSTS

FIG. 10c



1) PLACE PDMS MACROPOSTS

FIG. 11a



2) POUR PDMS AND PULL VACUUM

FIG. 11b

3) CURE AND REMOVE MACROPOSTS

FIG. 11c

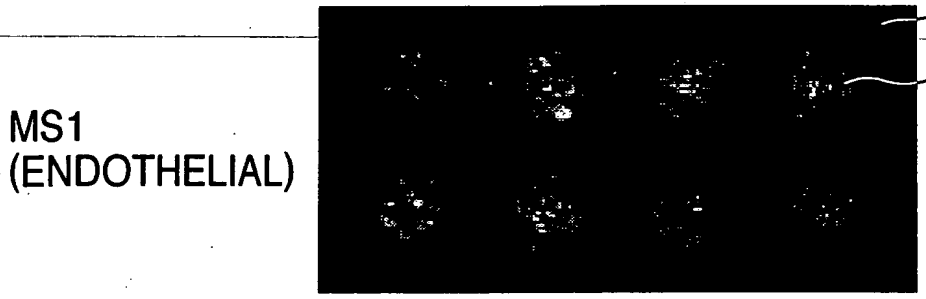


FIG. 12a

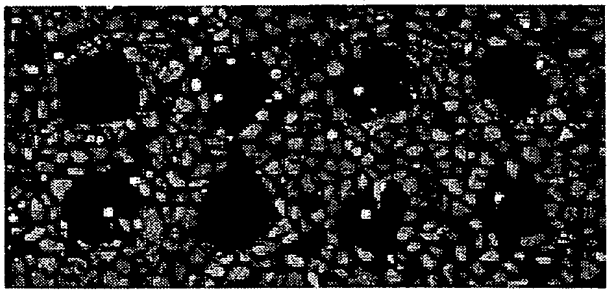


FIG. 12b

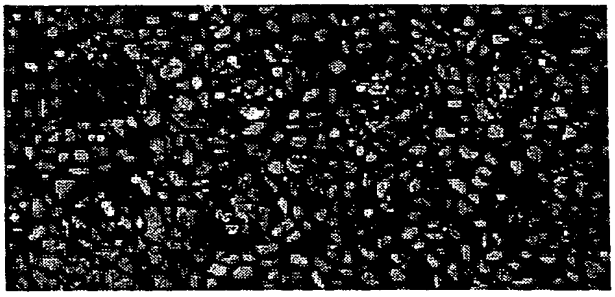
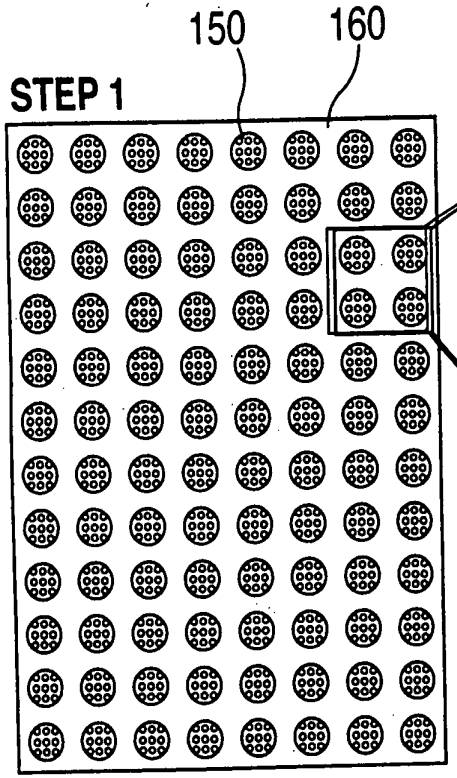


FIG. 12c



24-WELL OR
96-WELL FORMAT

FIG. 13a

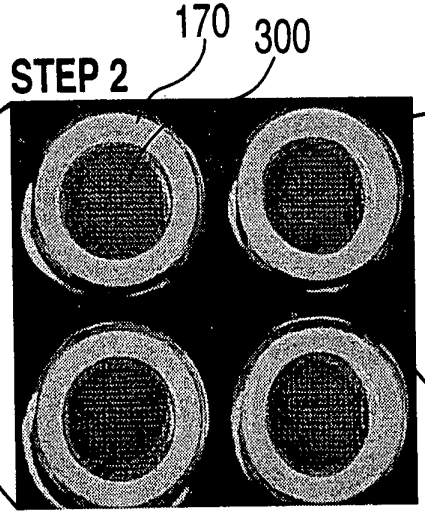


FIG. 13b

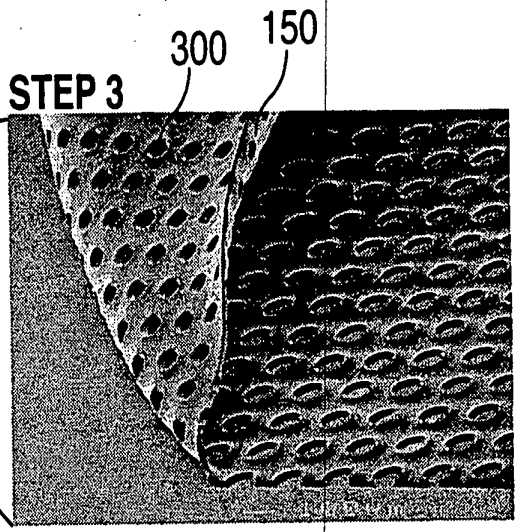


FIG. 13c

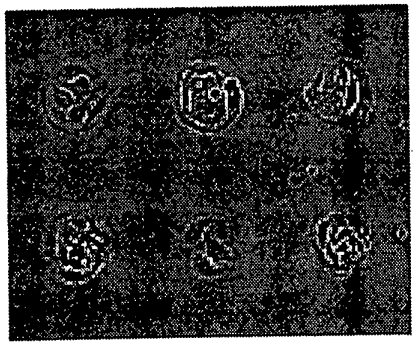


FIG. 13d

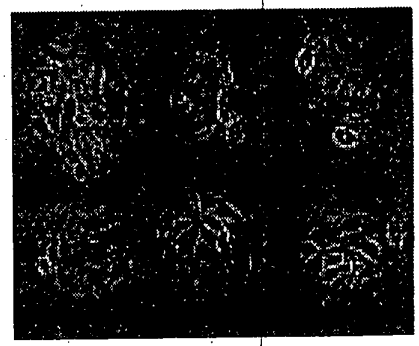
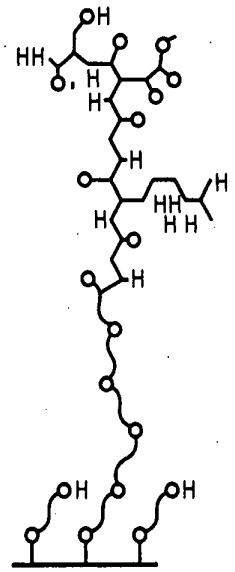
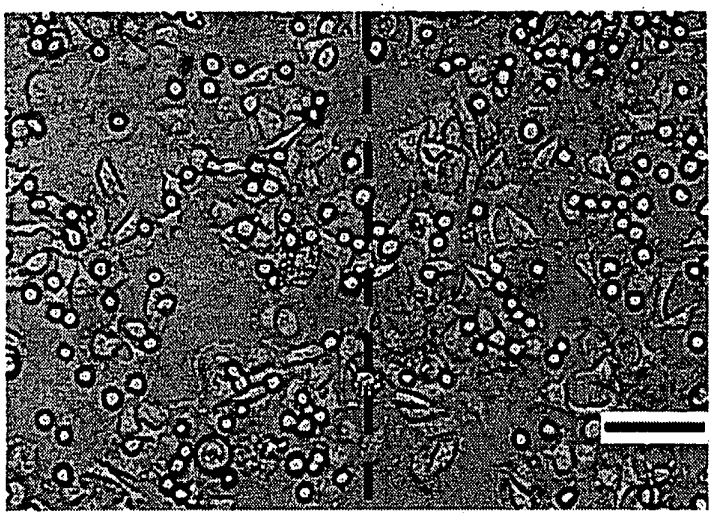


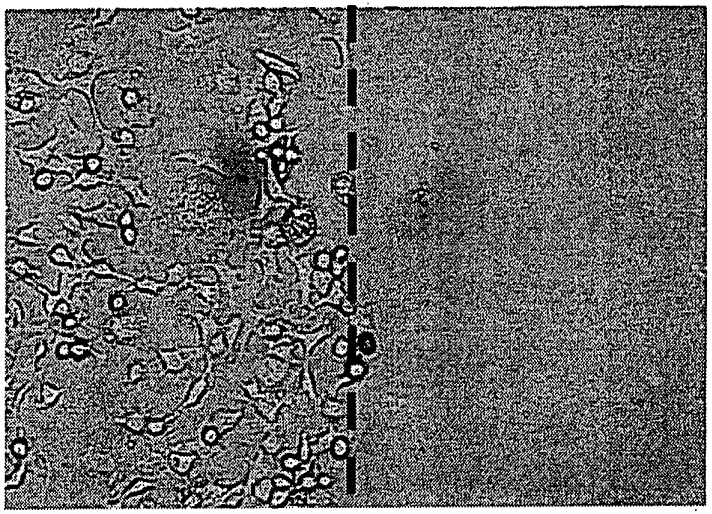
FIG. 13e

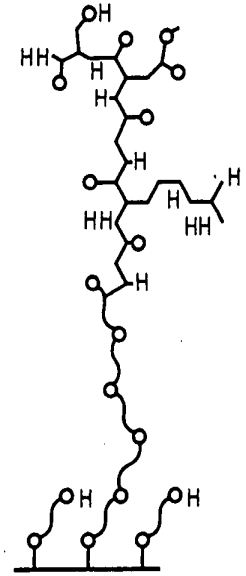
FIG. 14

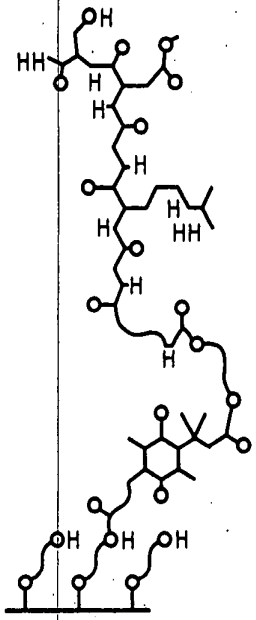


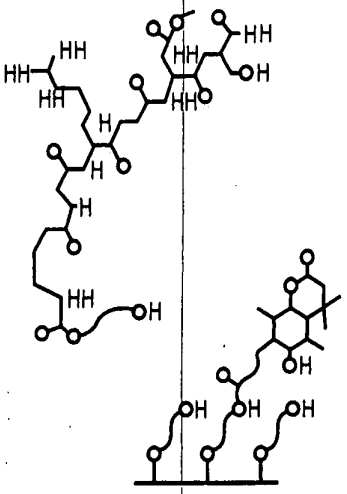


APPLY ELECTROCHEMICAL POTENTIAL









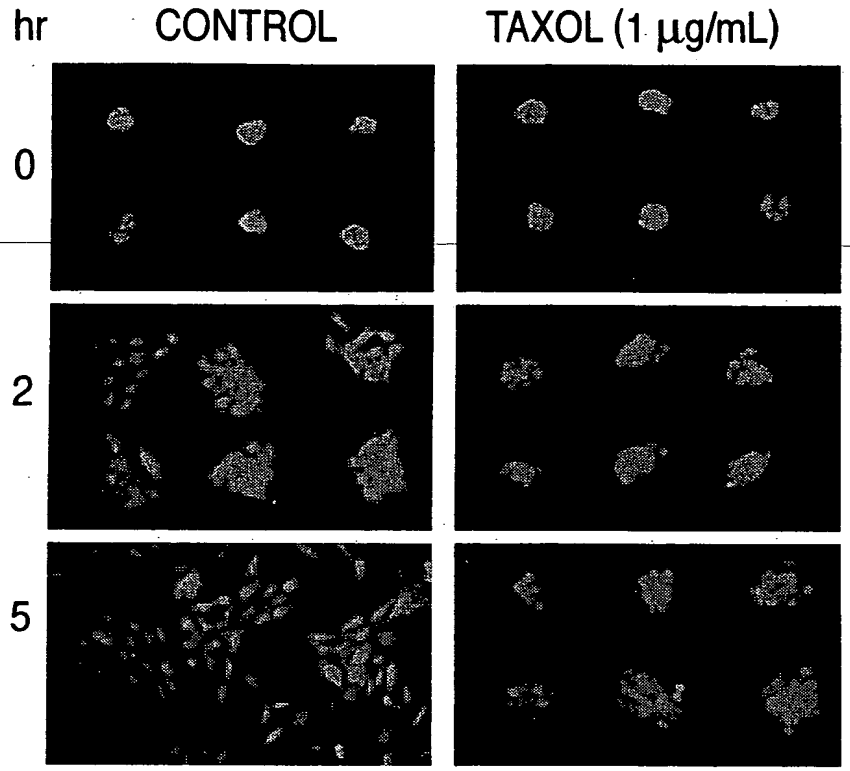


FIG. 15a

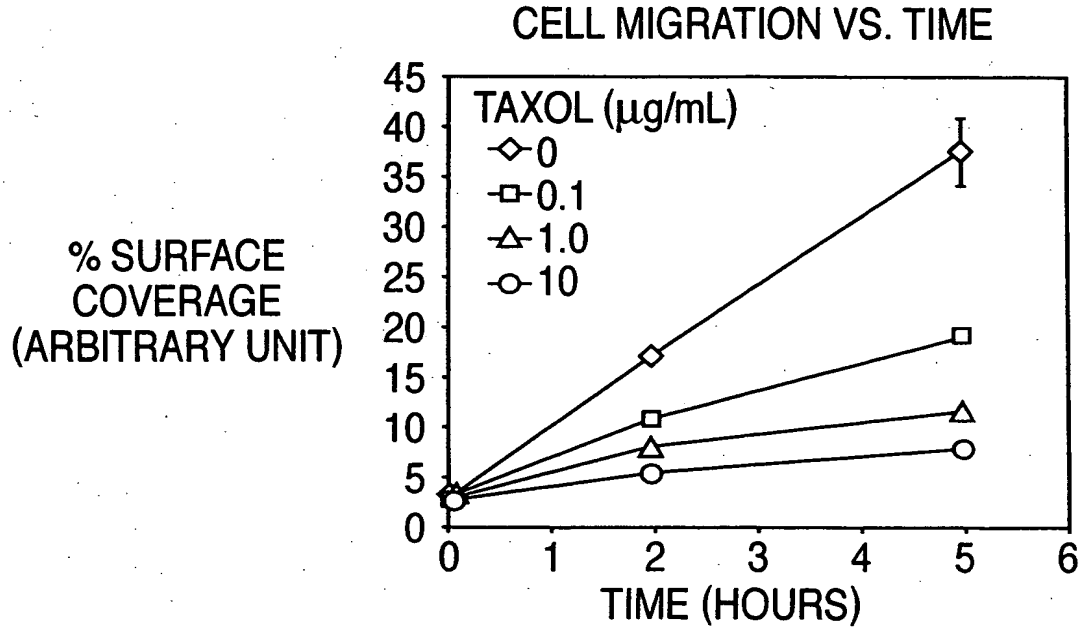


FIG. 15b

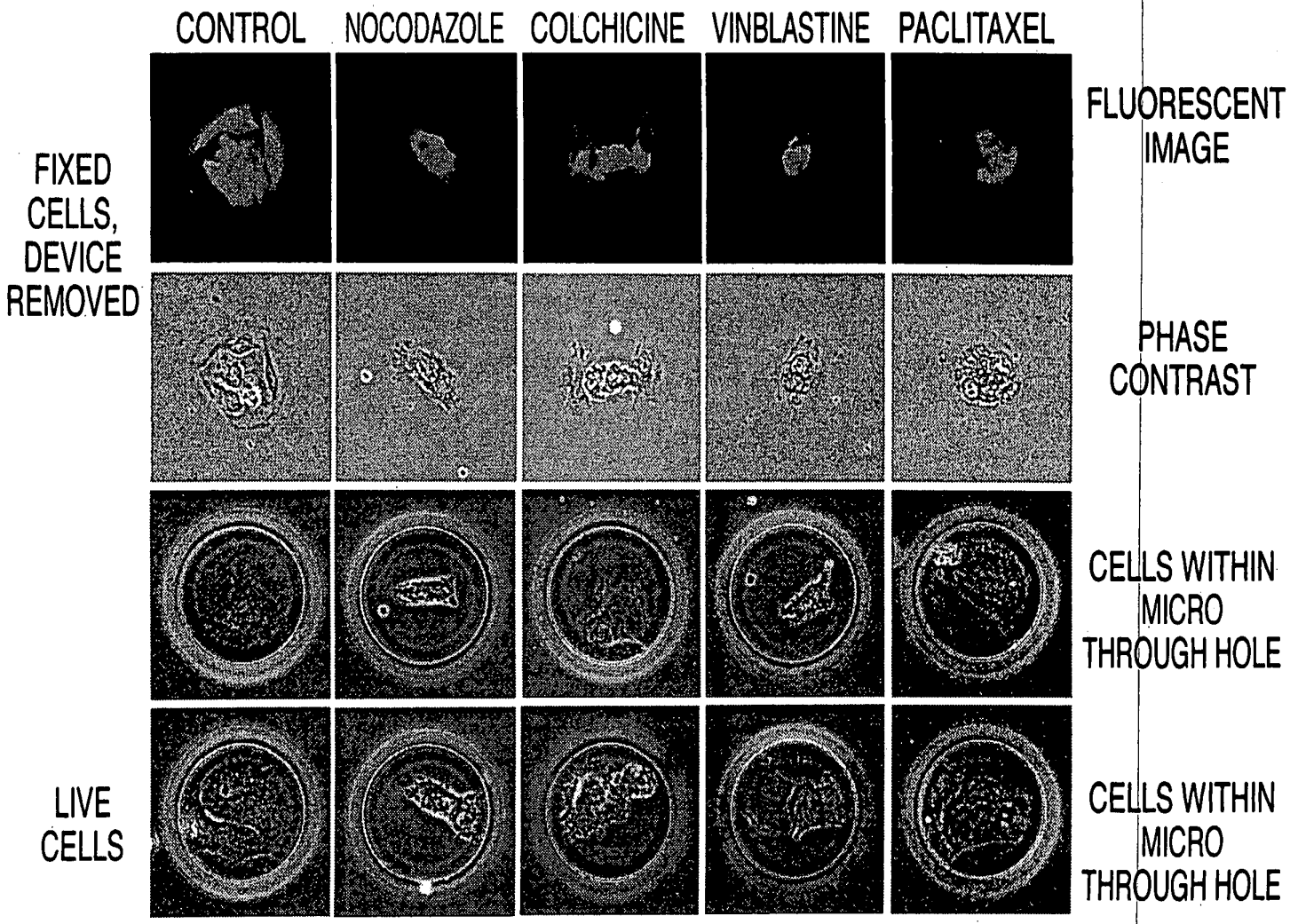

CONTROL
NOCODAZOLE
COLCHICINE
VINBLASTINE
PACLITAXEL
FIXED CELLS, DEVICE REMOVED
FLUORESCENT IMAGE
PHASE CONTRAST
CELLS WITHIN MICRO THROUGH HOLE
LIVE CELLS
CELLS WITHIN MICRO THROUGH HOLE

FIG. 16

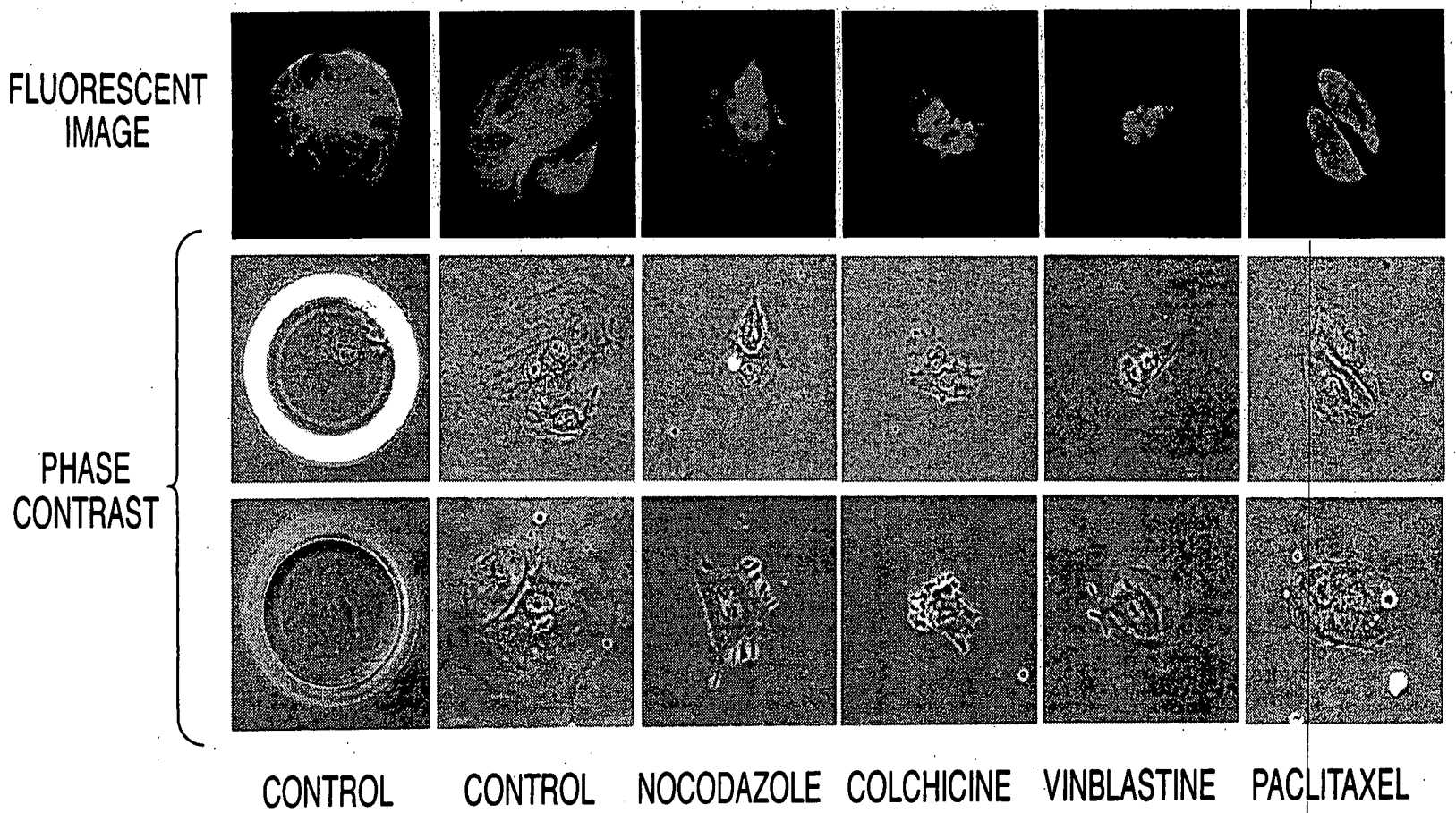

FLUORESCENT IMAGE
PHASE CONTRAST
CONTROL
CONTROL
NOCODAZOLE
COLCHICINE
VINBLASTINE
PACLITAXEL
DRUGS ADDED JUST PRIOR TO REMOVAL OF PATTERNING MEMBER

FIG. 17

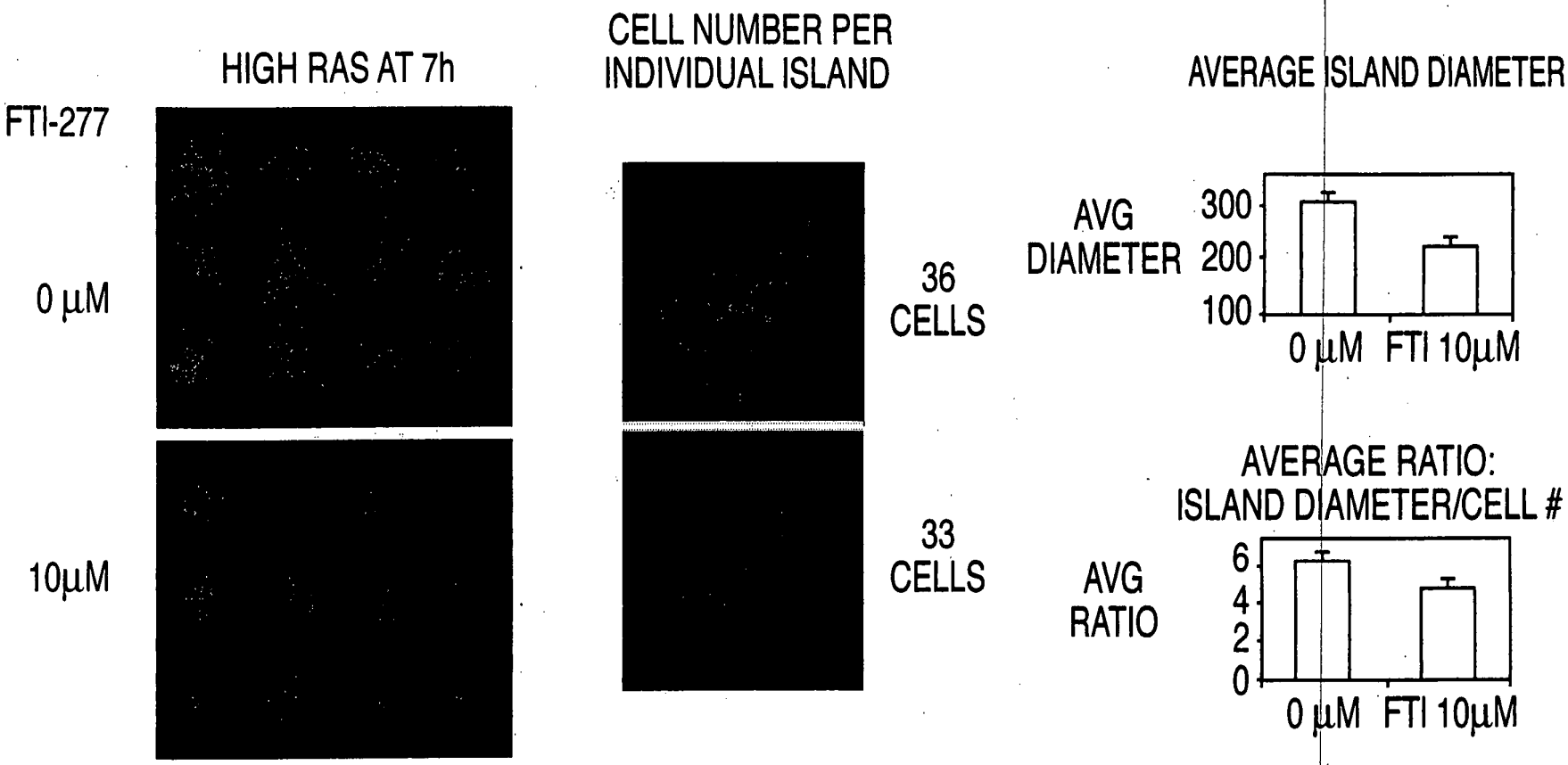

HIGH RAS AT 7h
CELL NUMBER PER INDIVIDUAL ISLAND
AVERAGE ISLAND DIAMETER
FTI-277
0 μM
10μM
36 CELLS
33 CELLS
AVG DIAMETER
300
200
100
0 μM
FTI 10μM
AVERAGE RATIO: ISLAND DIAMETER/CELL #
AVG RATIO
6
4
2
0
0 μM
FTI 10μM

FIG. 18

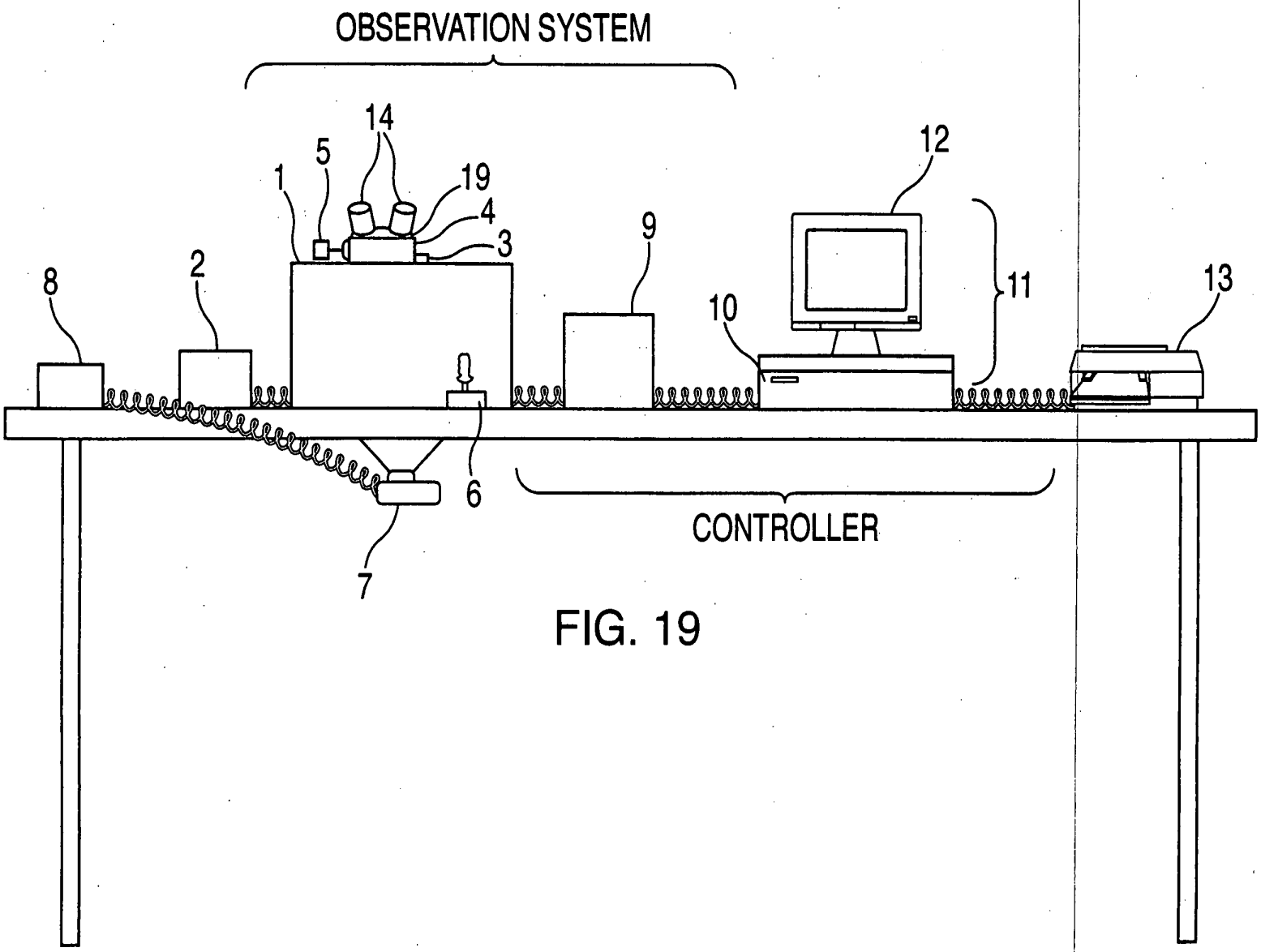


FIG. 19

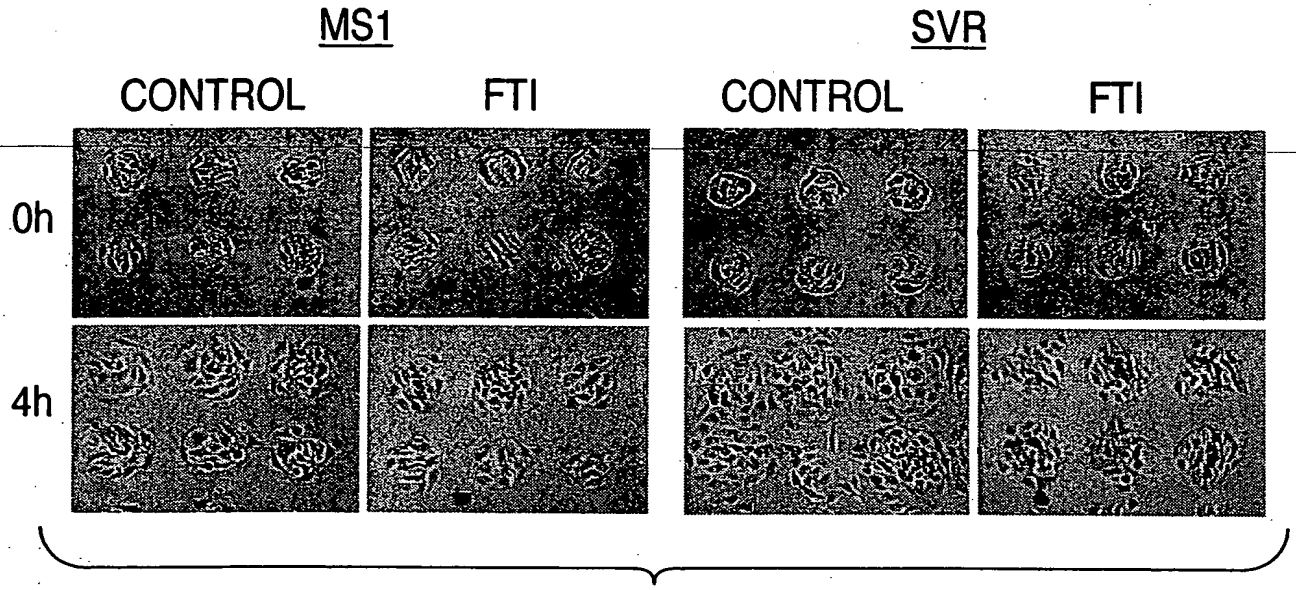

MS1
SVR
CONTROL
FTI
CONTROL
FTI
0h
4h

FIG. 20

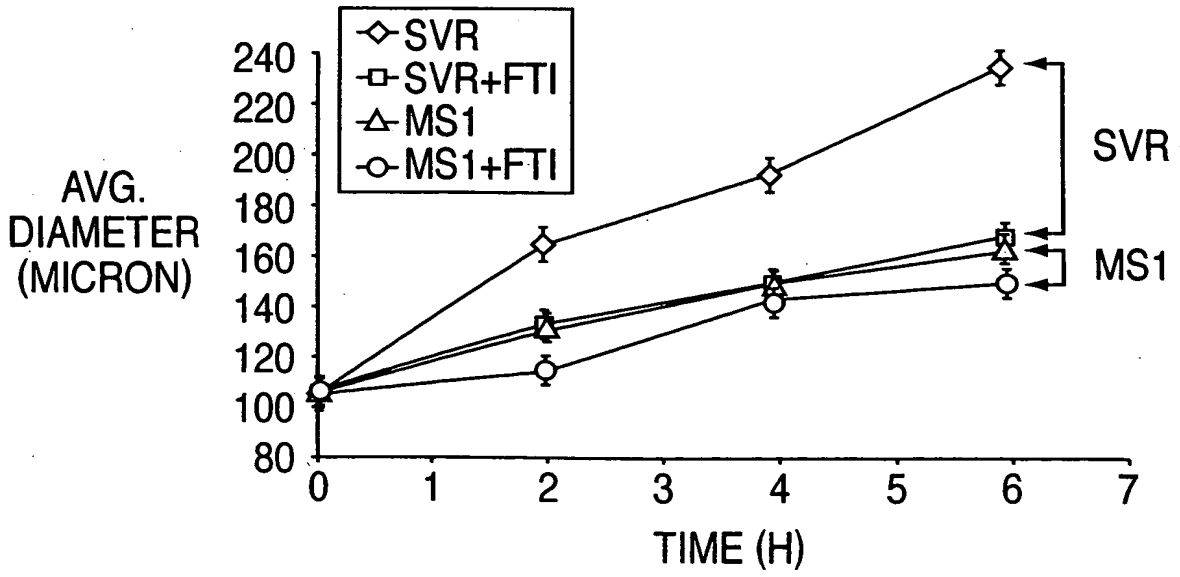

SVR
SVR+FTI
MS1
MS1+FTI
AVG. DIAMETER (MICRON)
240
220
200
180
160
140
120
100
80
0
1
2
3
4
5
6
7
TIME (H)
SVR
MS1

FIG. 21

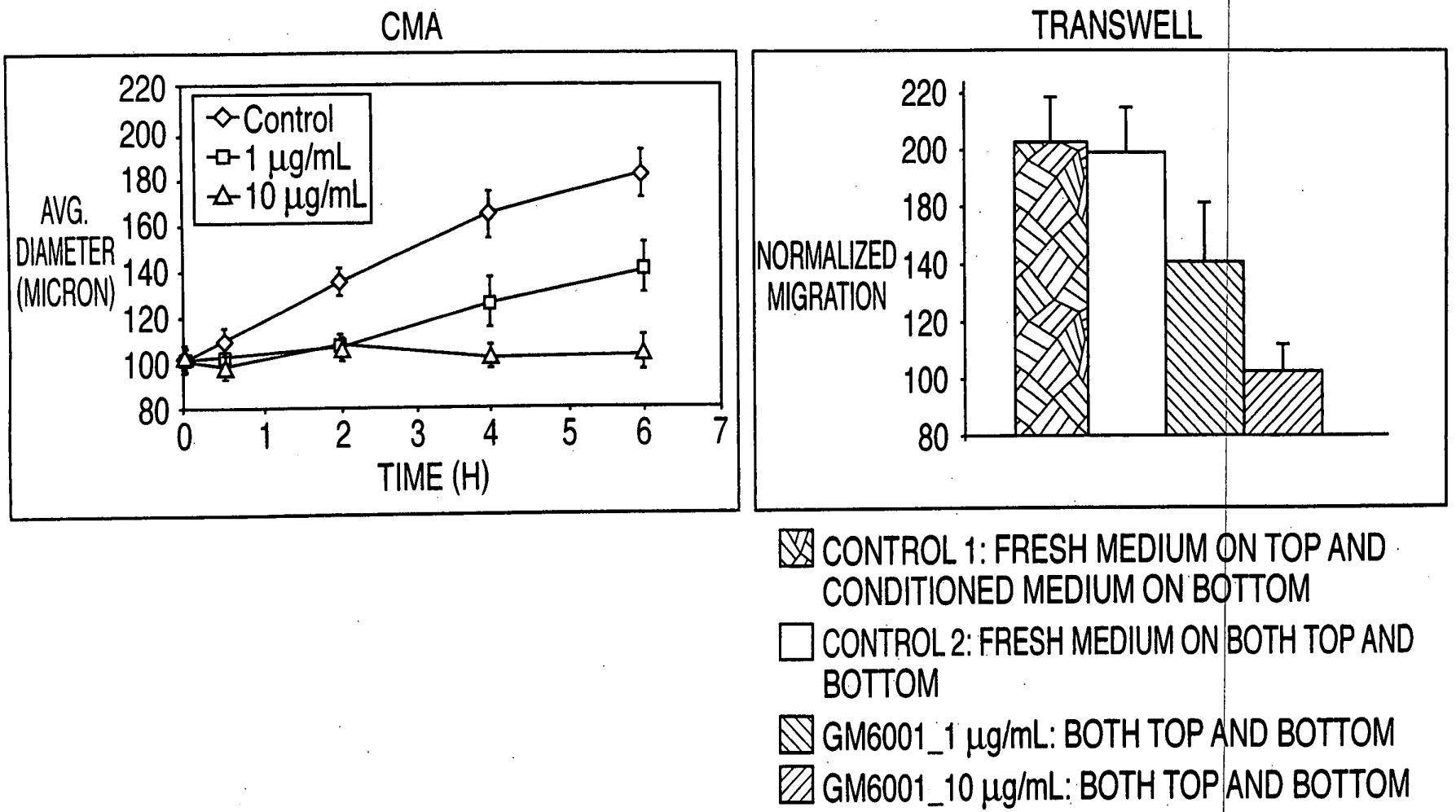
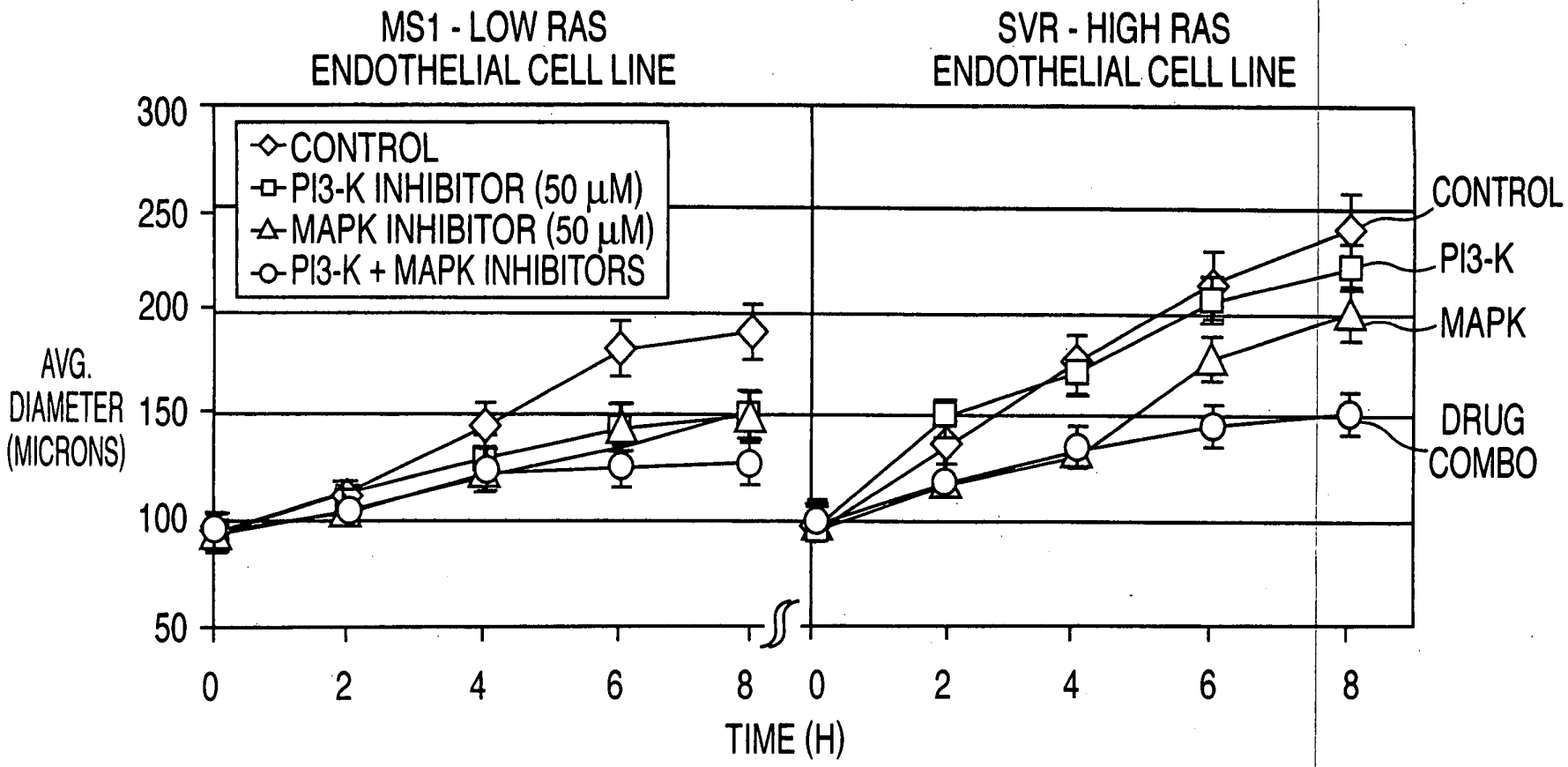

CMA
AVG. DIAMETER (MICRON)
220
200
180
160
140
120
100
80
Control
1 µg/mL
10 µg/mL
0
1
2
3
4
5
6
7
TIME (H)
TRANSWELL
NORMALIZED MIGRATION
220
200
180
140
120
100
80
CONTROL 1: FRESH MEDIUM ON TOP AND CONDITIONED MEDIUM ON BOTTOM
CONTROL 2: FRESH MEDIUM ON BOTH TOP AND BOTTOM
GM6001_1 µg/mL: BOTH TOP AND BOTTOM
GM6001_10 µg/mL: BOTH TOP AND BOTTOM

FIG. 22



- INHIBITION OF PI3-KINASE CAUSED A STRONGER INHIBITORY EFFECT IN MS1 (LOW RAS)
- INHIBITION USING BOTH PI3-K (LY90049) AND MAPK (PD98059) GENERATED AN ADDICTIVE SUPPRESSION OF MIGRATION

FIG. 23

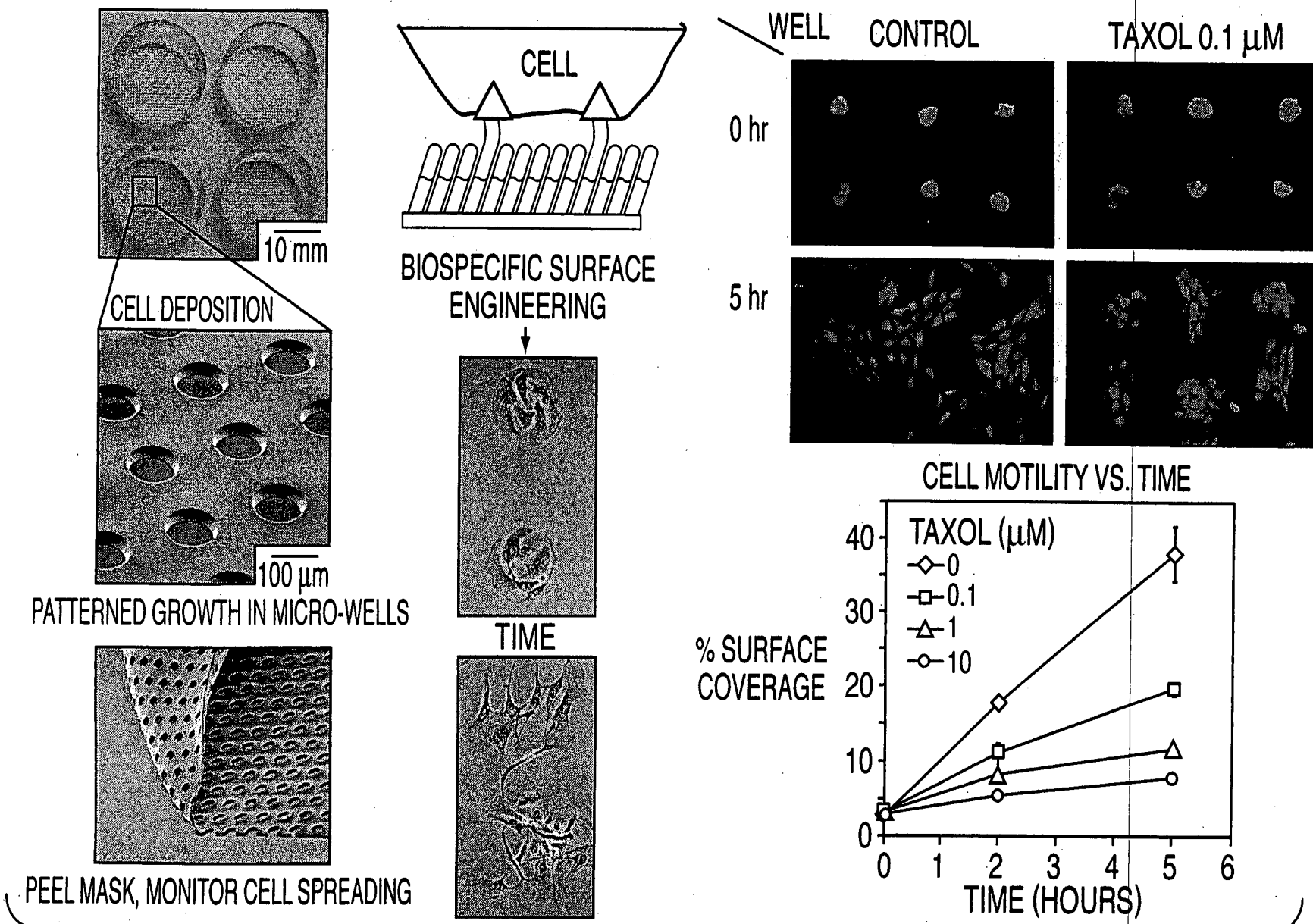

10 mm
CELL DEPOSITION
100 µm
PATTERNED GROWTH IN MICRO-WELLS
PEEL MASK, MONITOR CELL SPREADING
CELL
BIOSPECIFIC SURFACE ENGINEERING
TIME
WELL
CONTROL
TAXOL 0.1 µM
0 hr
5 hr
CELL MOTILITY VS. TIME
TAXOL (µM)
0
0.1
1
10
% SURFACE COVERAGE
TIME (HOURS)

FIG. 24

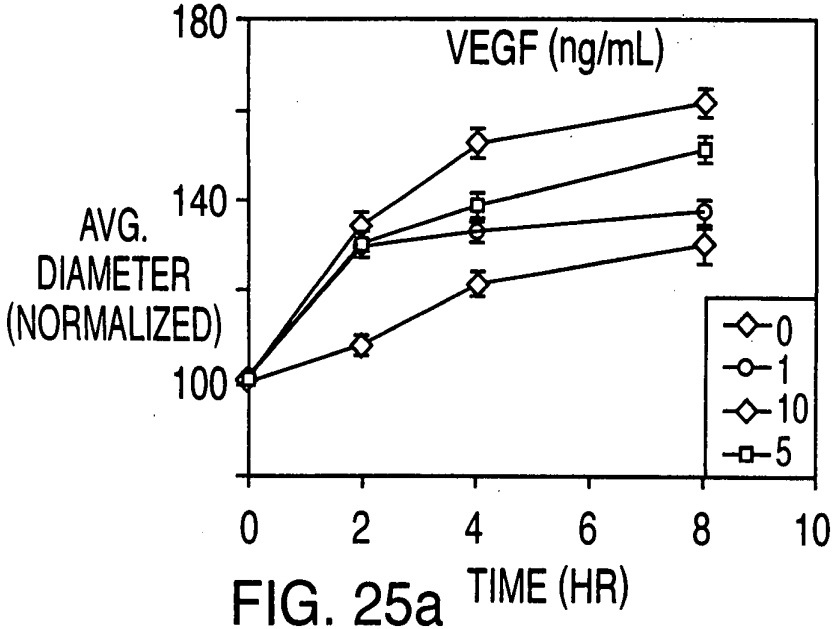


FIG. 25a

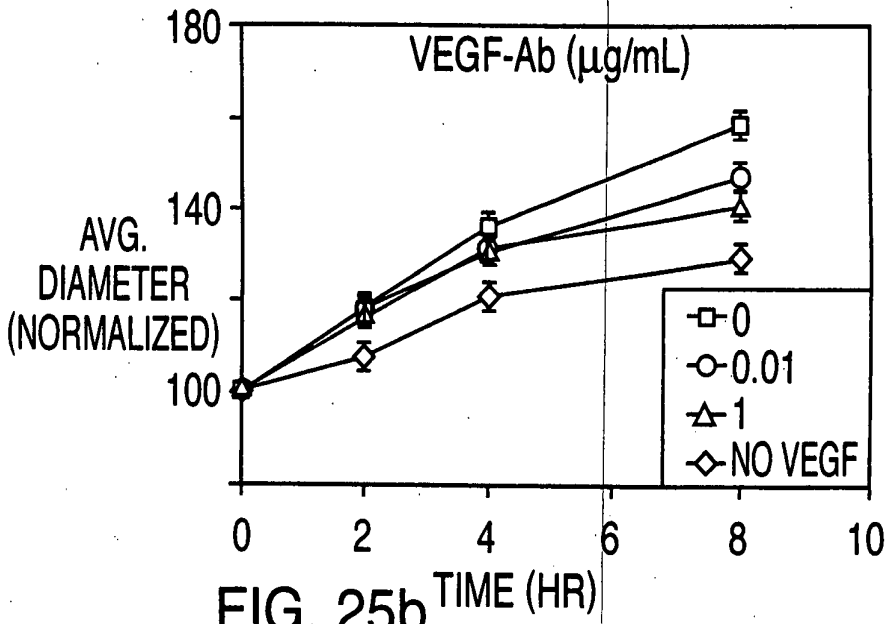


FIG. 25b

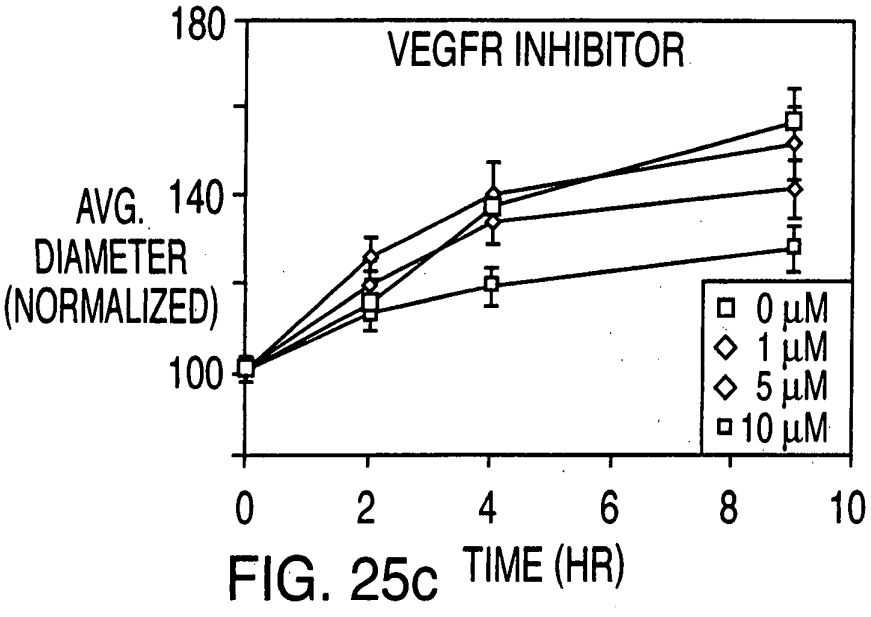


FIG. 25c

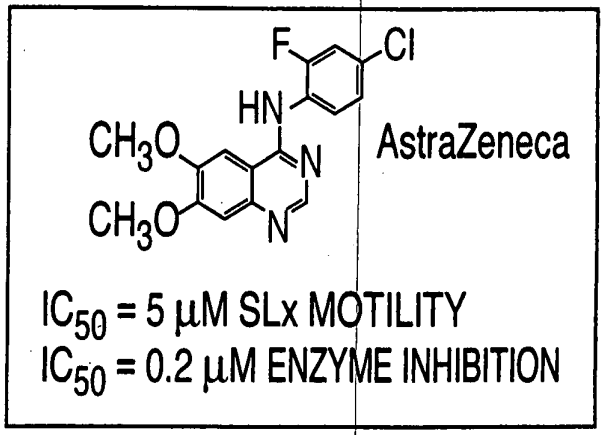
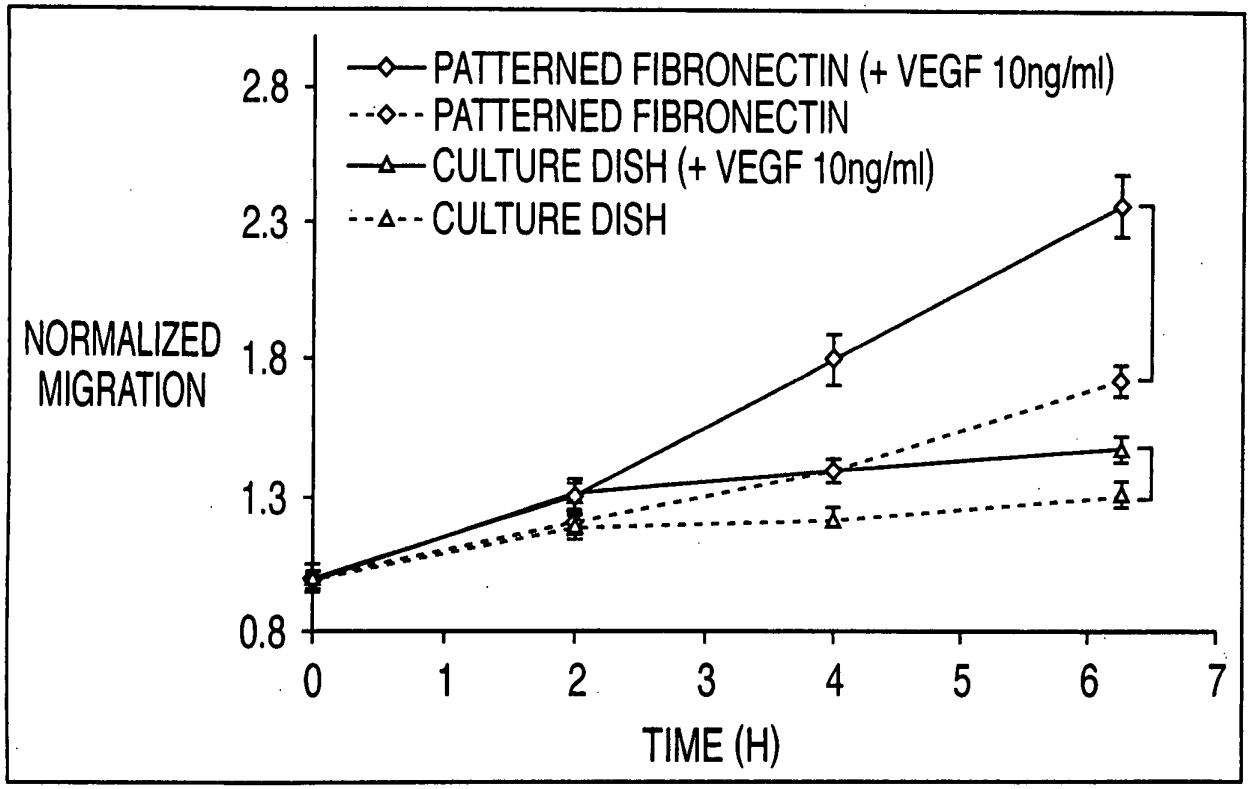
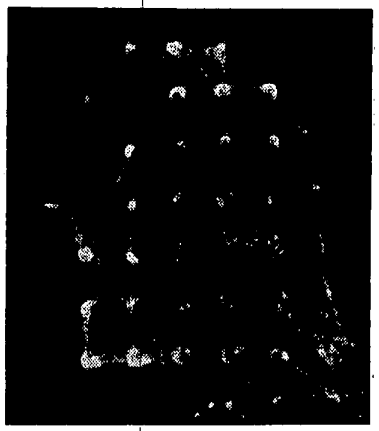


FIG. 25d

PATTERNED FIBRONECTIN VS TC PLASTIC



SURFACE - SPECIFIC CELLULAR RESPONSE USING FOCAL ADHESION MICROPATTERNING

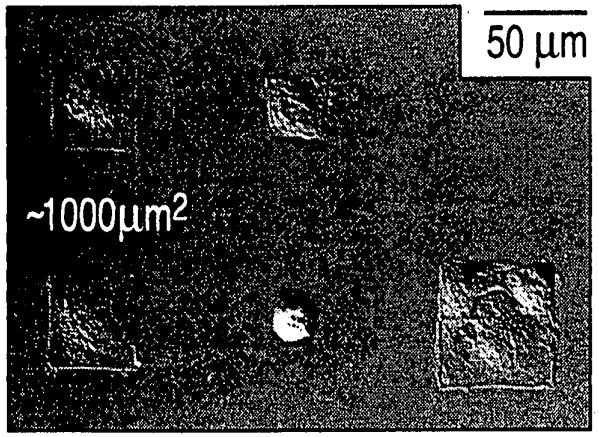


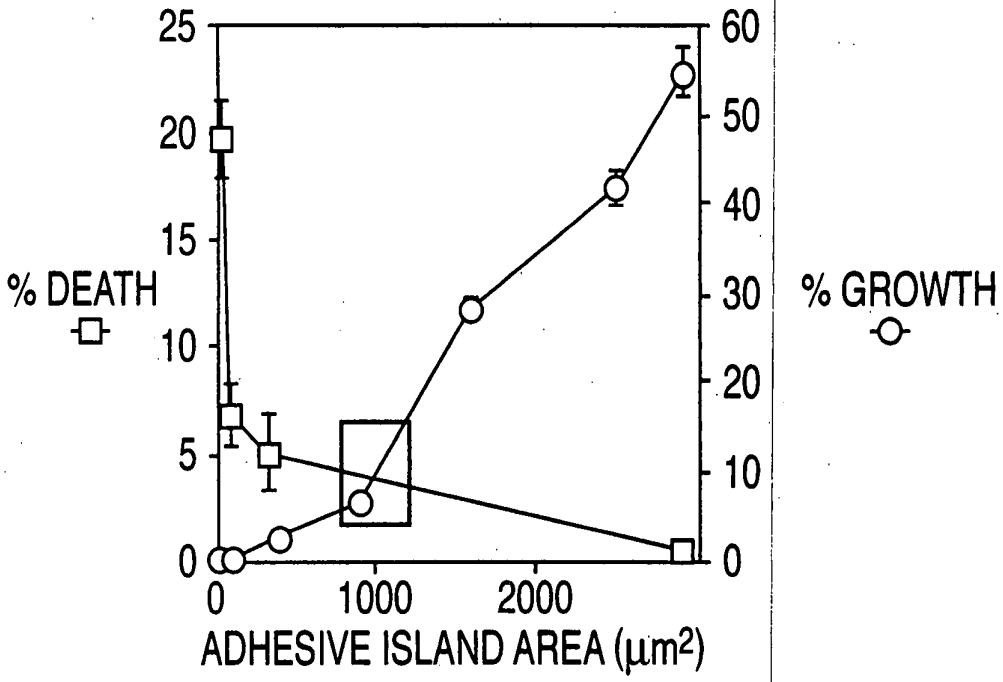
ACTIN

VINCULIN

SURFACE CHEMISTRY AND MICROCONTACT PRINTING LEAD TO MORE ROBUST MOTILITY MEASUREMENTS

FIG. 26





- ATTACHMENT AREA DETERMINES PHYSIOLOGICAL STATE
- PREPARATION OF HOMOGENOUS POPULATIONS OF CELLS

CELL CONTROL FROM 1000 µm²

- CELL CYCLE ENTRY-GROWTH
- ONSET OF APOPTOTIC CASCADE
- SWITCH TO DIFFERENTIATION

FIG. 27

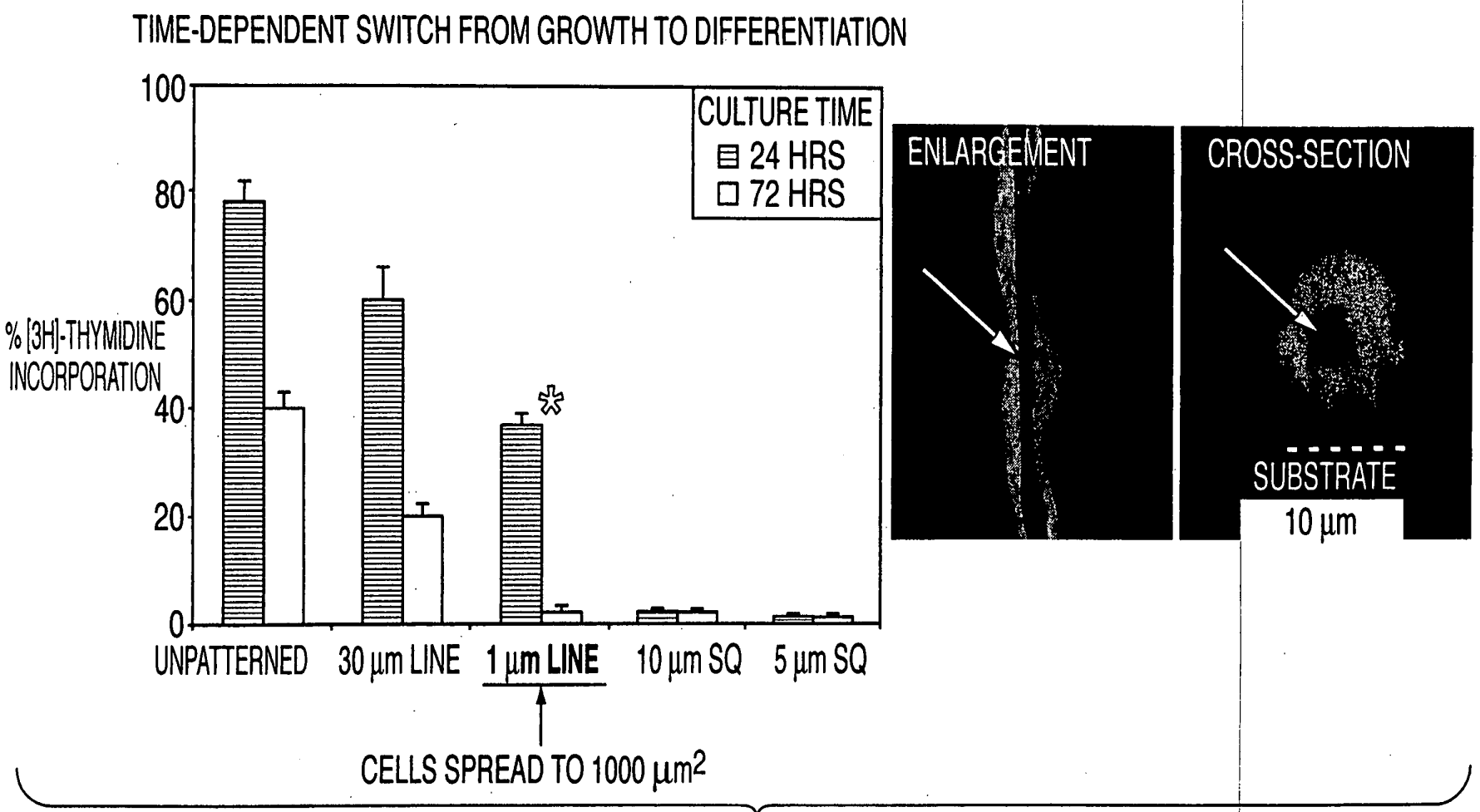
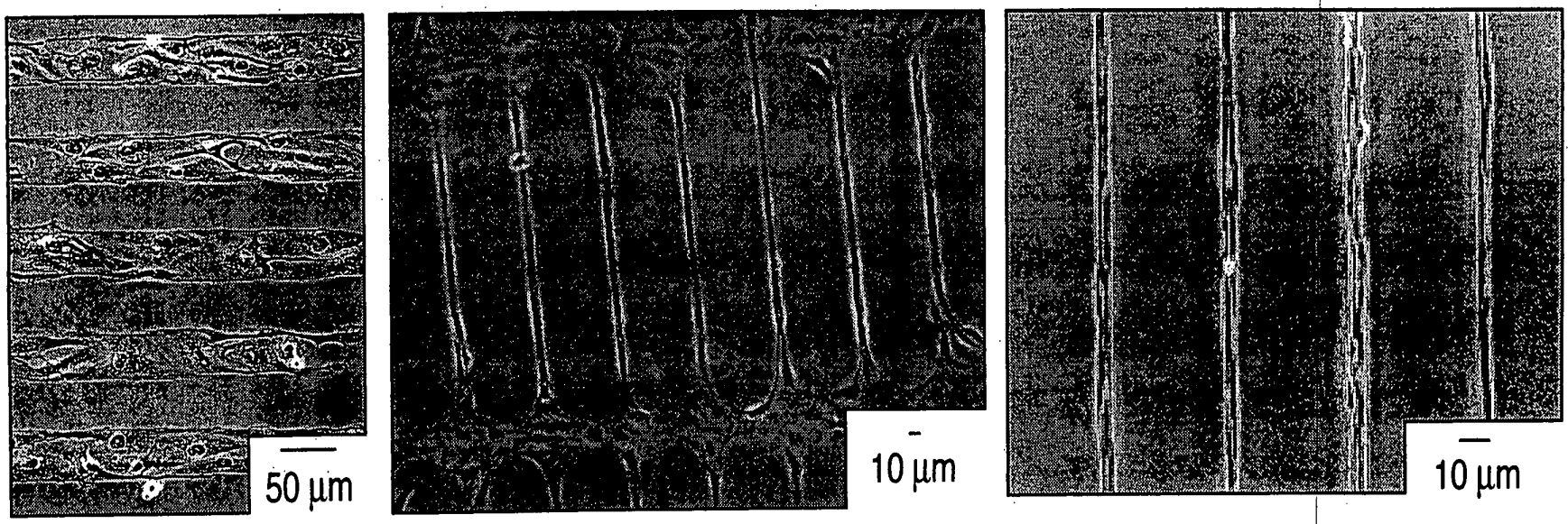

TIME-DEPENDENT SWITCH FROM GROWTH TO DIFFERENTIATION
100
80
60
40
20
0
% [3H]-THYMIDINE INCORPORATION
CULTURE TIME
24 HRS
72 HRS
UNPATTERNED
30 μm LINE
1 μm LINE
10 μm SQ
5 μm SQ
CELLS SPREAD TO 1000 μm2
ENLARGEMENT
CROSS-SECTION
SUBSTRATE
10 μm

FIG. 28



- ALIGNMENT
- POLARIZATION
- GROWTH

→

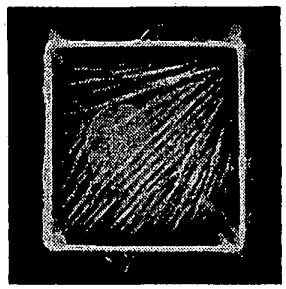
- ALIGNMENT
- POLARIZATION
- SIZE REDUCTION
- ARRAY

→

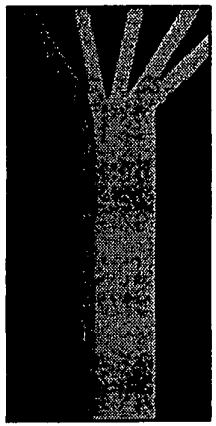
- ALIGNMENT
- POLARIZATION
- DIFFERENTIATION ARRAY

FIG. 29

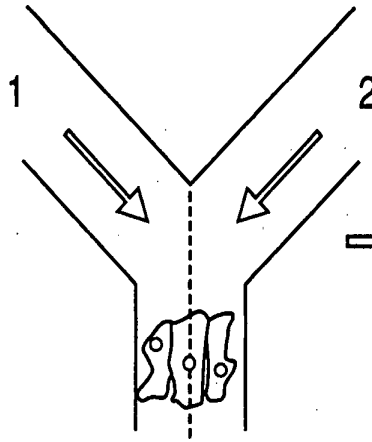
EVALUATION OF CYTOSKELETAL STABILITY AND REARRANGEMENT

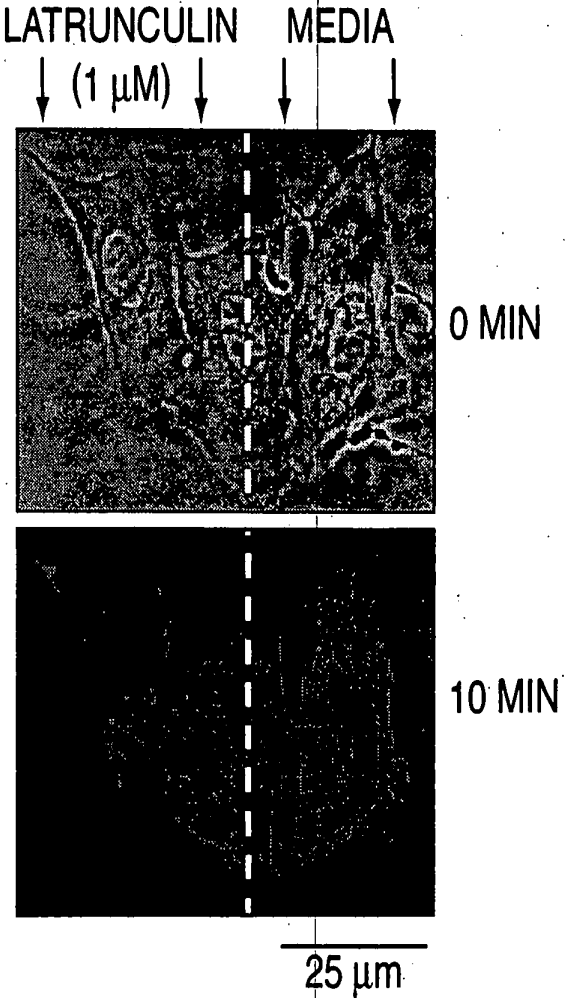


SINGLE CELL PATTERNING



GRADIENT GENERATION





ACTIN STAINING AFTER TREATMENT

FIG. 30

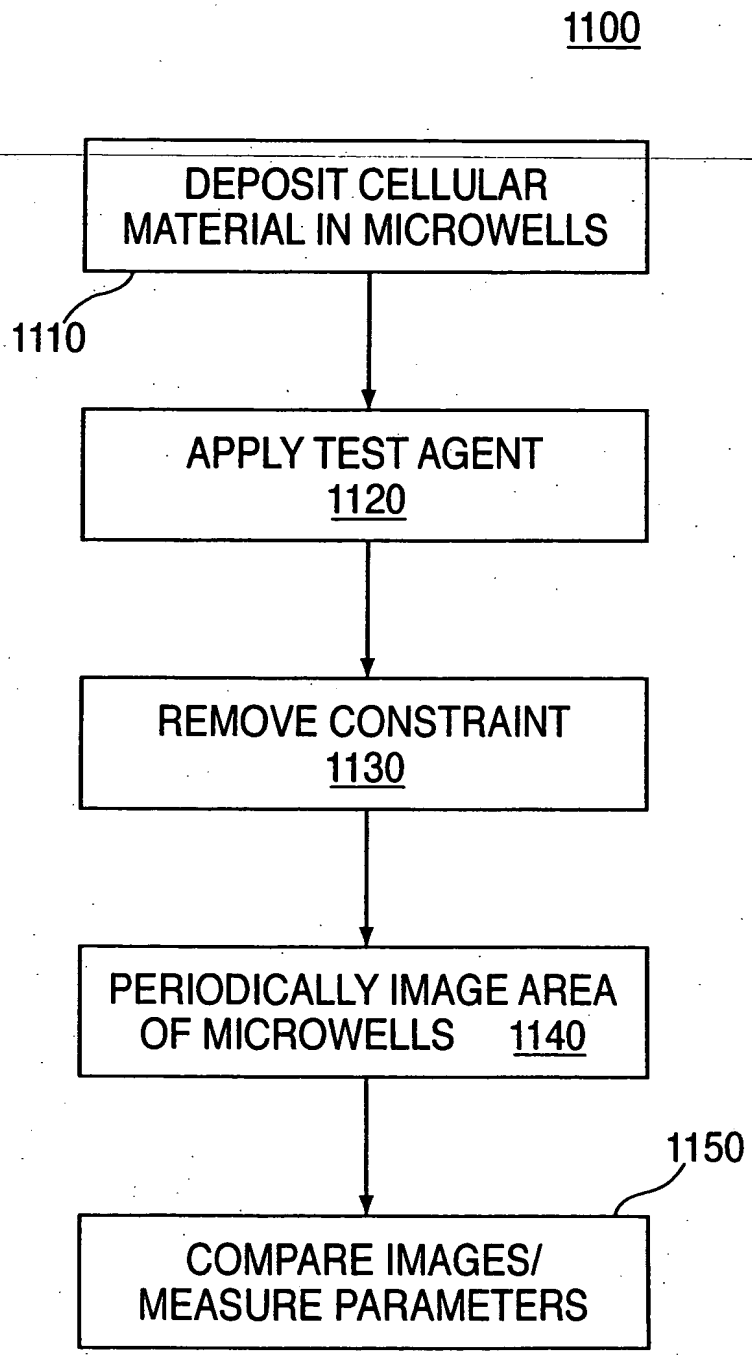

1100
DEPOSIT CELLULAR MATERIAL IN MICROWELLS
1110
APPLY TEST AGENT 1120
REMOVE CONSTRAINT 1130
PERIODICALLY IMAGE AREA OF MICROWELLS 1140
1150
COMPARE IMAGES/ MEASURE PARAMETERS

FIG. 31

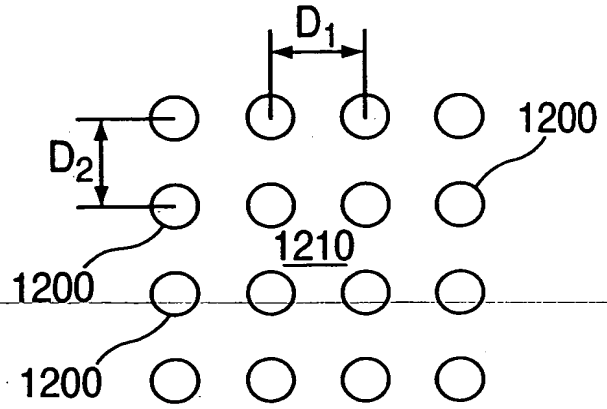


FIG. 32

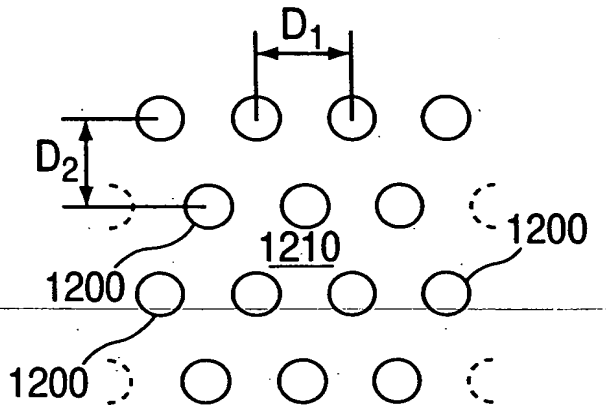


FIG. 33

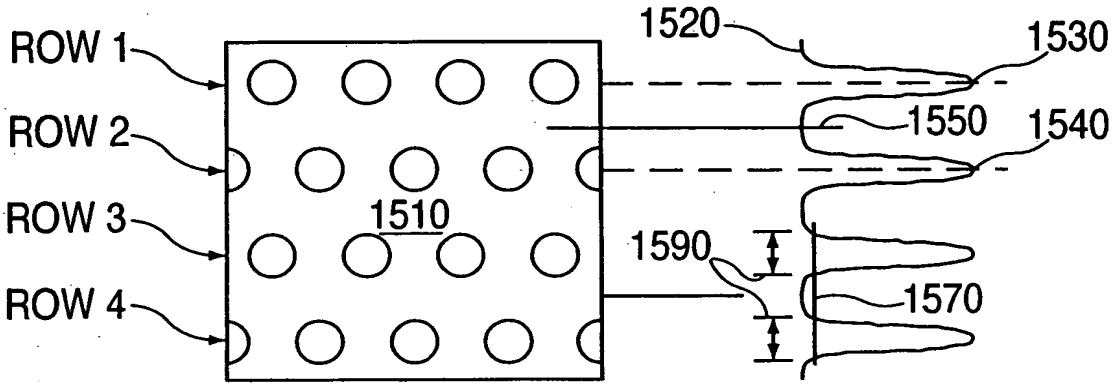


FIG. 35

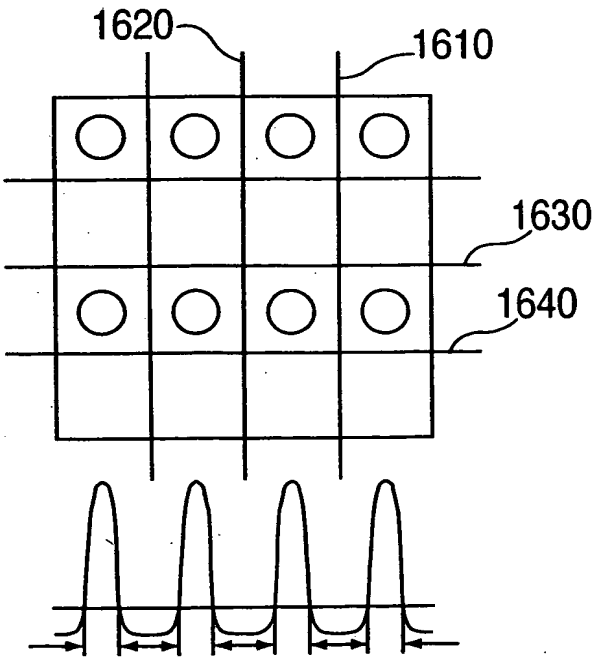


FIG. 36

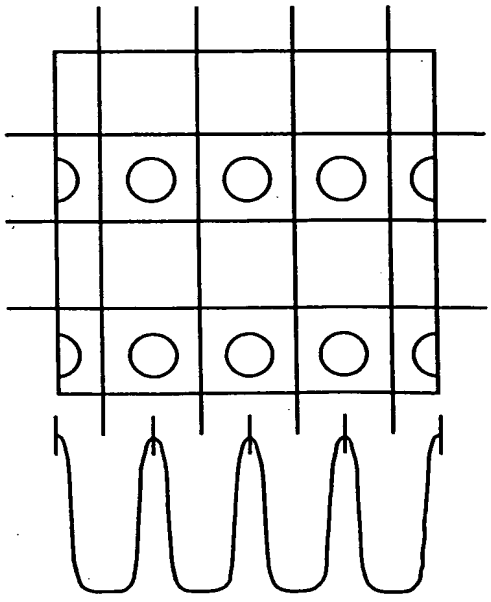


FIG. 37

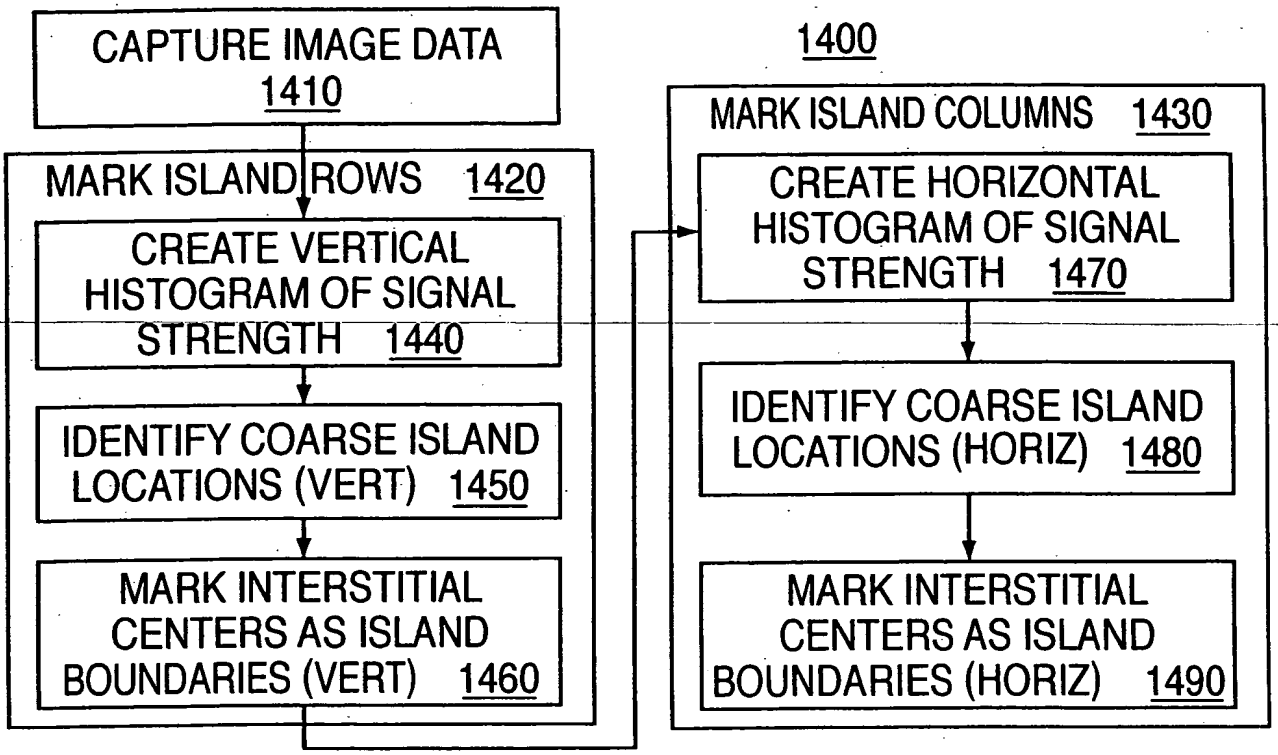

CAPTURE IMAGE DATA 1410
1400
MARK ISLAND ROWS 1420
CREATE VERTICAL HISTOGRAM OF SIGNAL STRENGTH 1440
IDENTIFY COARSE ISLAND LOCATIONS (VERT) 1450
MARK INTERSTITIAL CENTERS AS ISLAND BOUNDARIES (VERT) 1460
MARK ISLAND COLUMNS 1430
CREATE HORIZONTAL HISTOGRAM OF SIGNAL STRENGTH 1470
IDENTIFY COARSE ISLAND LOCATIONS (HORIZ) 1480
MARK INTERSTITIAL CENTERS AS ISLAND BOUNDARIES (HORIZ) 1490

FIG. 34

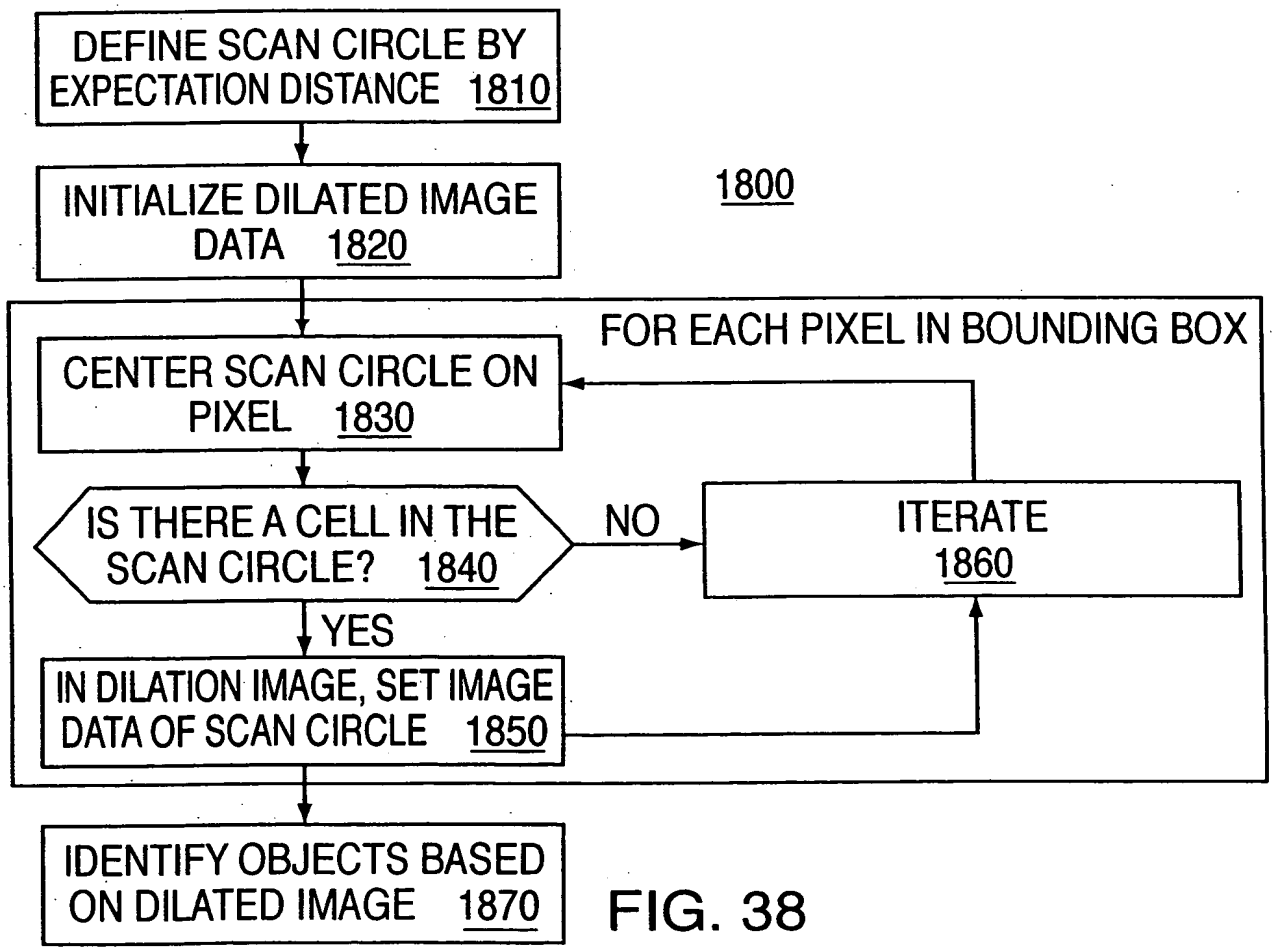

DEFINE SCAN CIRCLE BY EXPECTATION DISTANCE 1810
INITIALIZE DILATED IMAGE DATA 1820
1800
FOR EACH PIXEL IN BOUNDING BOX
CENTER SCAN CIRCLE ON PIXEL 1830
IS THERE A CELL IN THE SCAN CIRCLE? 1840
NO
ITERATE 1860
YES
IN DILATION IMAGE, SET IMAGE DATA OF SCAN CIRCLE 1850
IDENTIFY OBJECTS BASED ON DILATED IMAGE 1870

FIG. 38

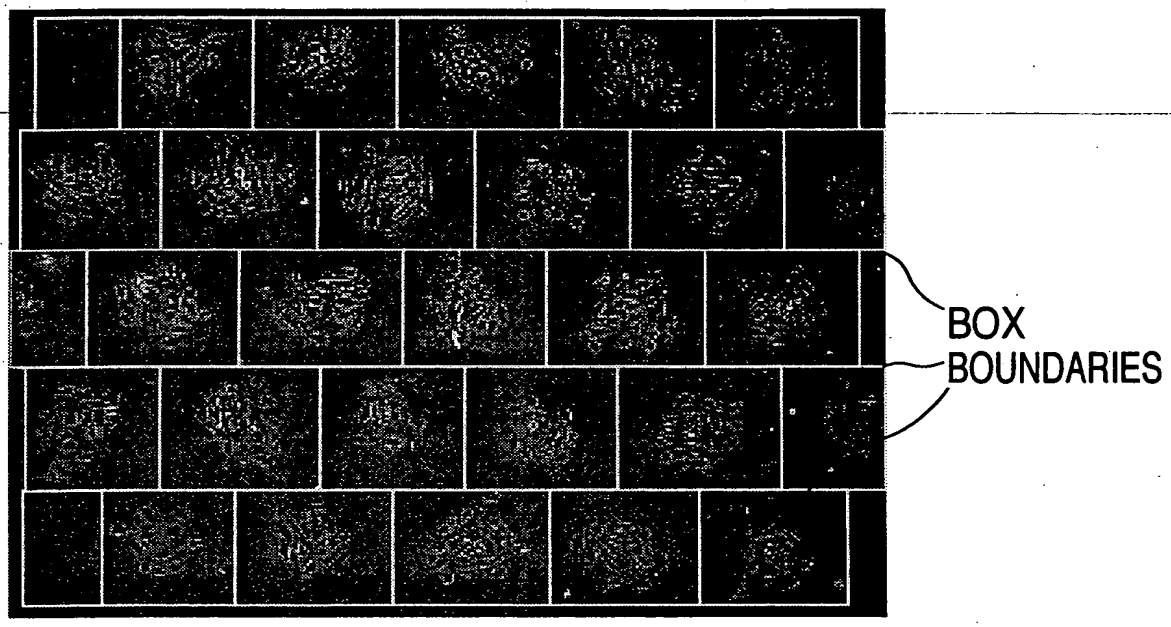


FIG. 39

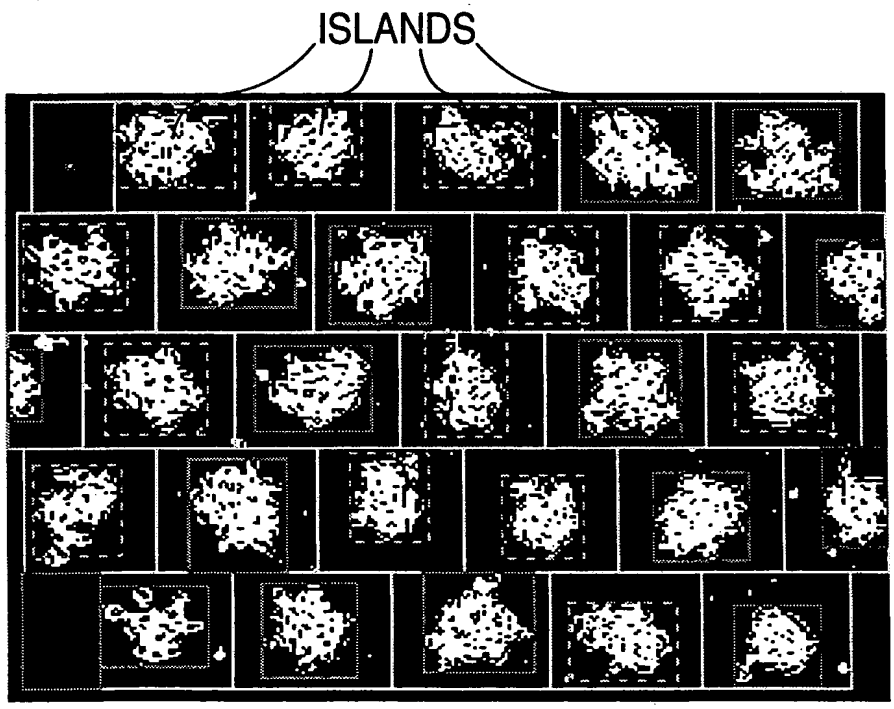


FIG. 40

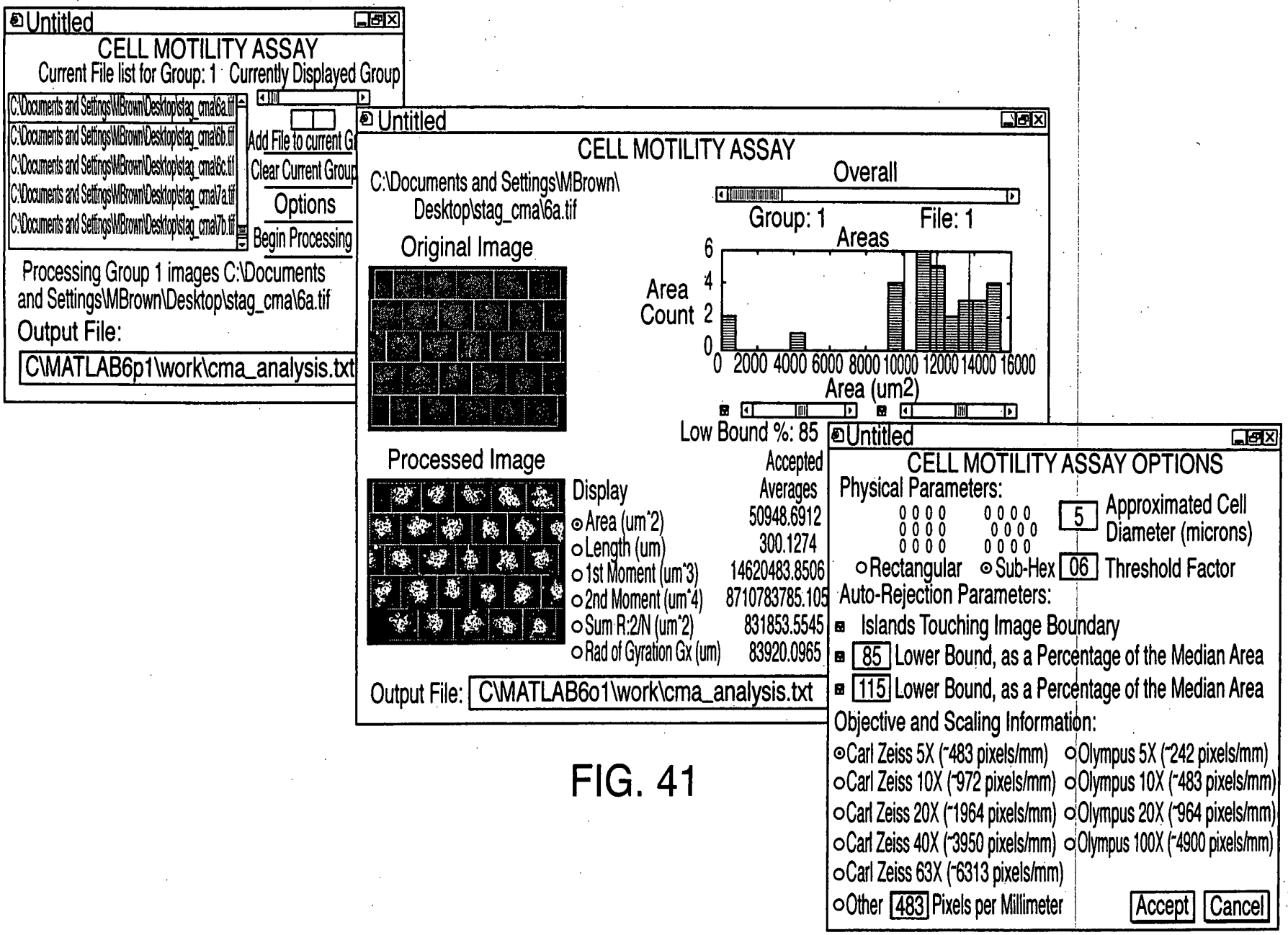

Untitled
CELL MOTILITY ASSAY
Current File list for Group: 1 Currently Displayed Group
C:\Documents and Settings\MBrown\Desktop\stag_cma\6a.tif
C:\Documents and Settings\MBrown\Desktop\stag_cma\6b.tif
C:\Documents and Settings\MBrown\Desktop\stag_cma\6c.tif
C:\Documents and Settings\MBrown\Desktop\stag_cma\7a.tif
C:\Documents and Settings\MBrown\Desktop\stag_cma\7b.tif
Add File to current G
Clear Current Group
Options
Begin Processing
Processing Group 1 images C:\Documents and Settings\MBrown\Desktop\stag_cma\6a.tif
Output File:
C\MATLAB6p1\work\cma_analysis.txt
Untitled
CELL MOTILITY ASSAY
C:\Documents and Settings\MBrown\Desktop\stag_cma\6a.tif
Overall
Group: 1
File: 1
Original Image
Areas
Area Count
6
4
2
0
0 2000 4000 6000 8000 10000 12000 14000 16000
Area (um2)
Low Bound %: 85
Processed Image
Display
Accepted Averages
Area (um^2) 50948.6912
Length (um) 300.1274
1st Moment (um^3) 14620483.8506
2nd Moment (um^4) 8710783785.105
Sum R:2/N (um^2) 831853.5545
Rad of Gyration Gx (um) 83920.0965
Output File: C\MATLAB6o1\work\cma_analysis.txt
Untitled
CELL MOTILITY ASSAY OPTIONS
Physical Parameters:
5 Approximated Cell Diameter (microns)
Rectangular
Sub-Hex
06 Threshold Factor
Auto-Rejection Parameters:
Islands Touching Image Boundary
85 Lower Bound, as a Percentage of the Median Area
115 Lower Bound, as a Percentage of the Median Area
Objective and Scaling Information:
Carl Zeiss 5X (~483 pixels/mm)
Olympus 5X (~242 pixels/mm)
Carl Zeiss 10X (~972 pixels/mm)
Olympus 10X (~483 pixels/mm)
Carl Zeiss 20X (~1964 pixels/mm)
Olympus 20X (~964 pixels/mm)
Carl Zeiss 40X (~3950 pixels/mm)
Olympus 100X (~4900 pixels/mm)
Carl Zeiss 63X (~6313 pixels/mm)
Other 483 Pixels per Millimeter
Accept
Cancel

FIG. 41

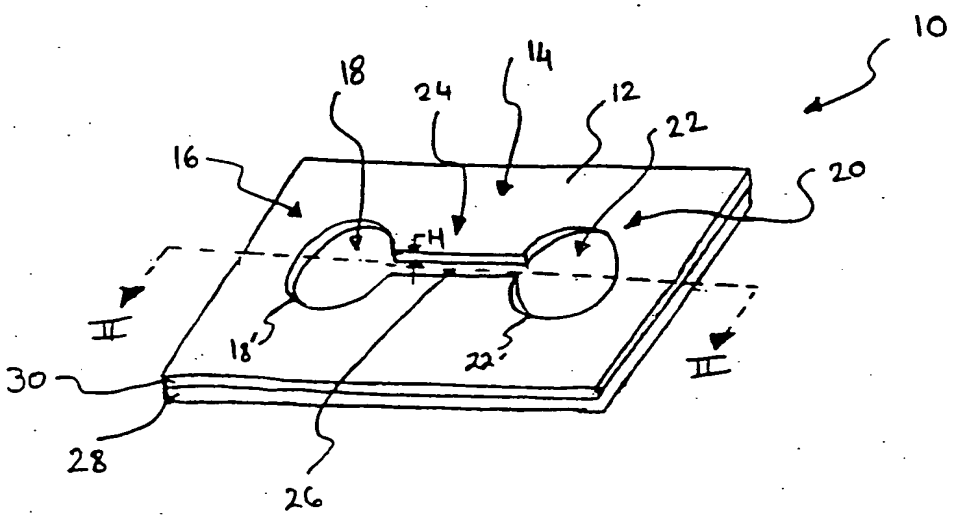


FIG. 42

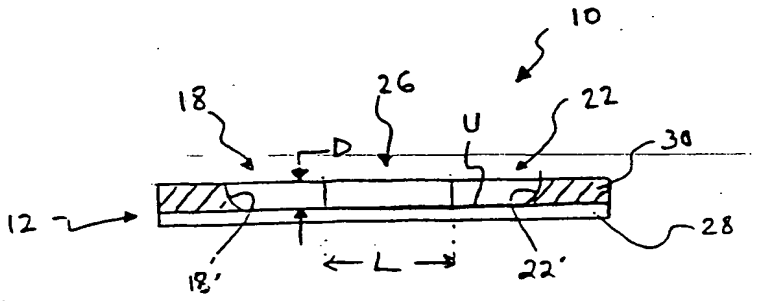


FIG. 43

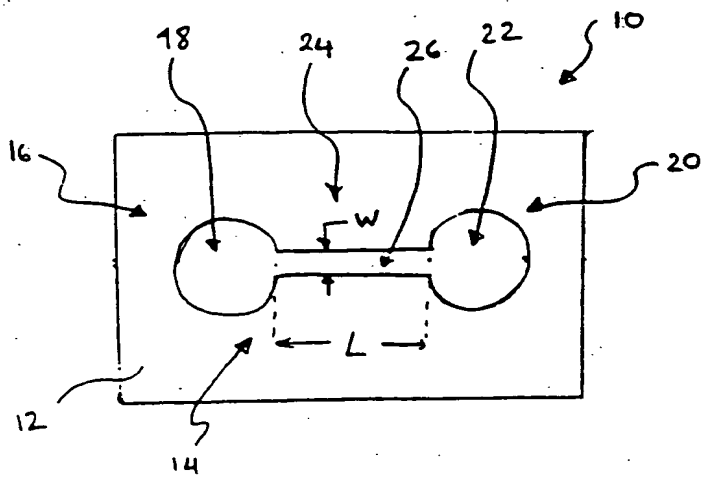


FIG. 44

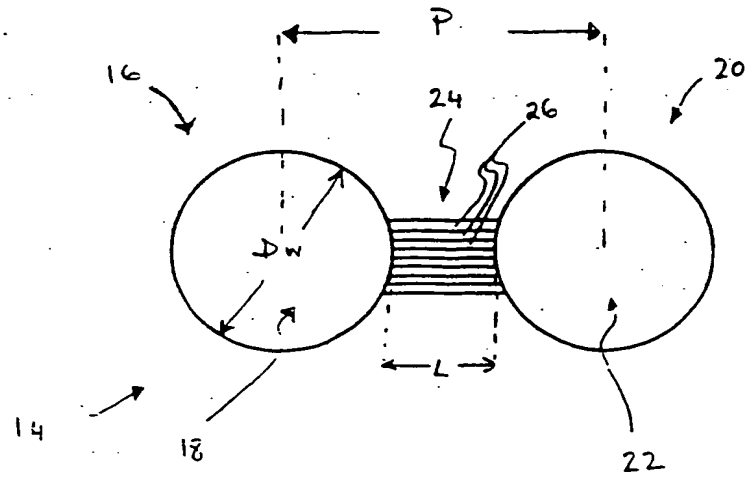


FIG. 45

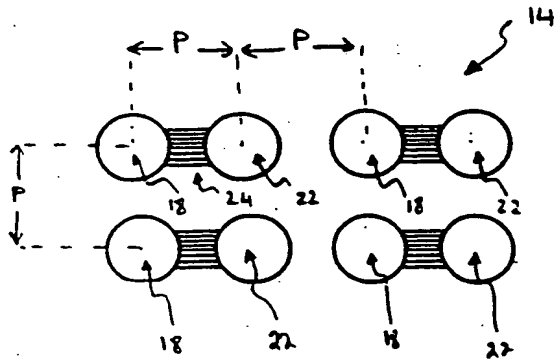


FIG. 46

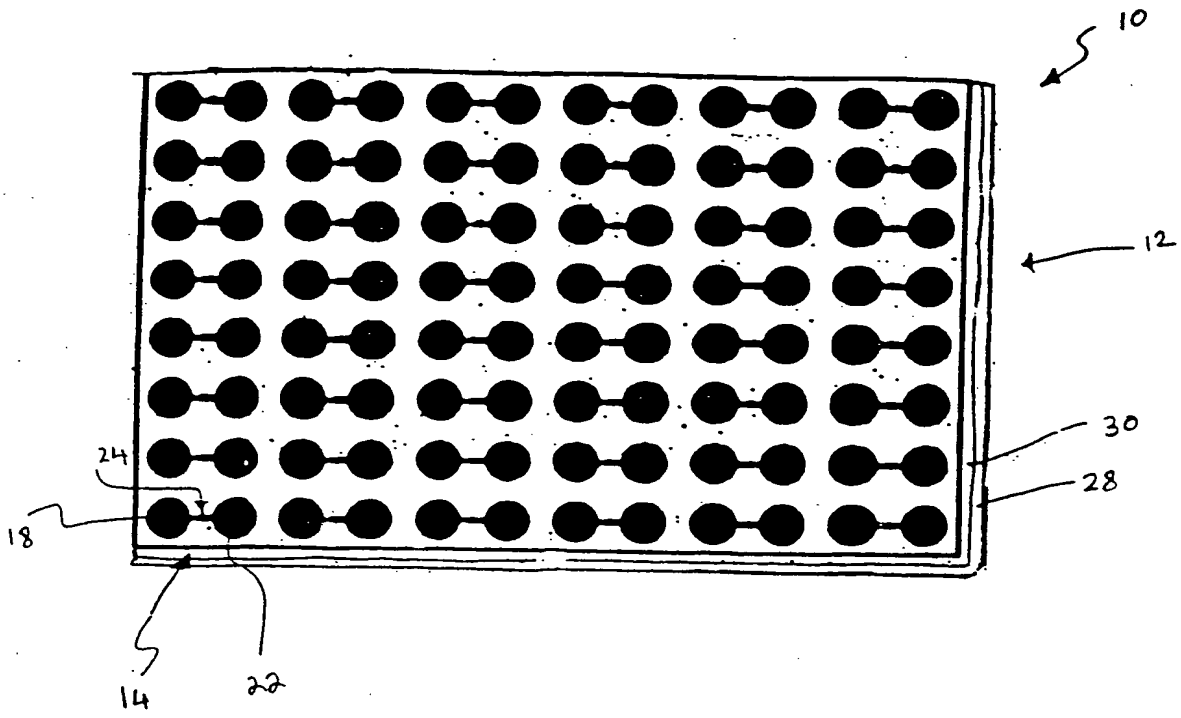
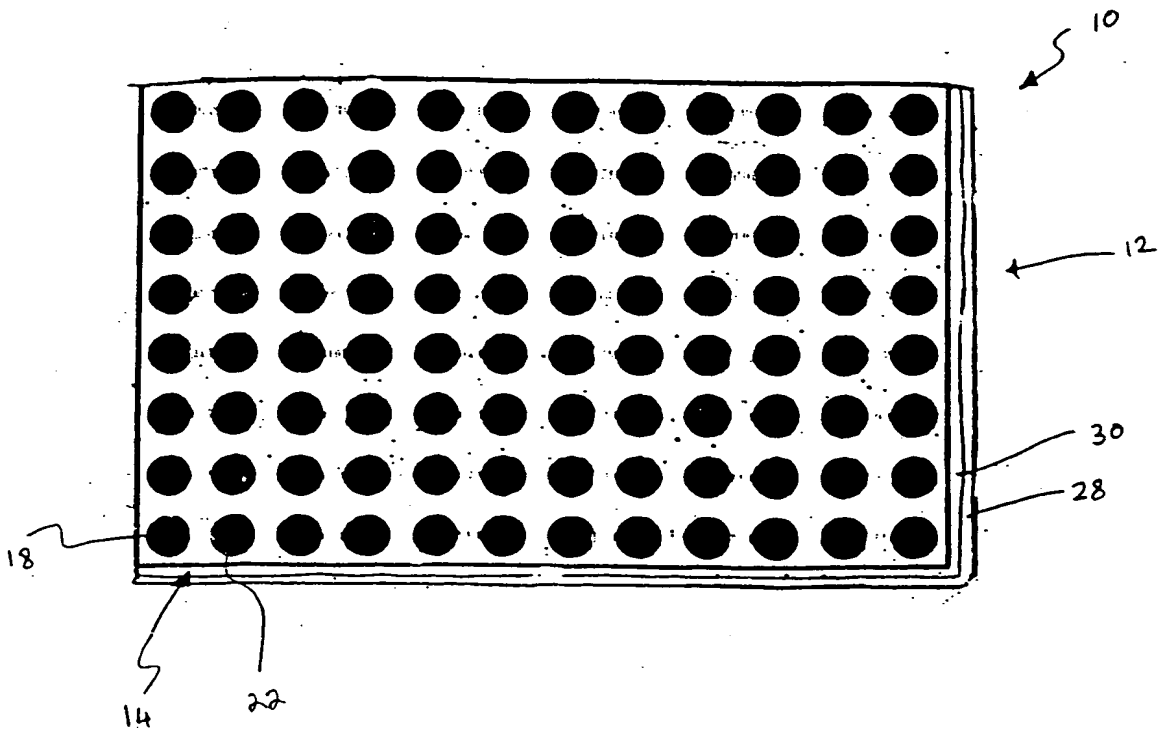


FIG. 47



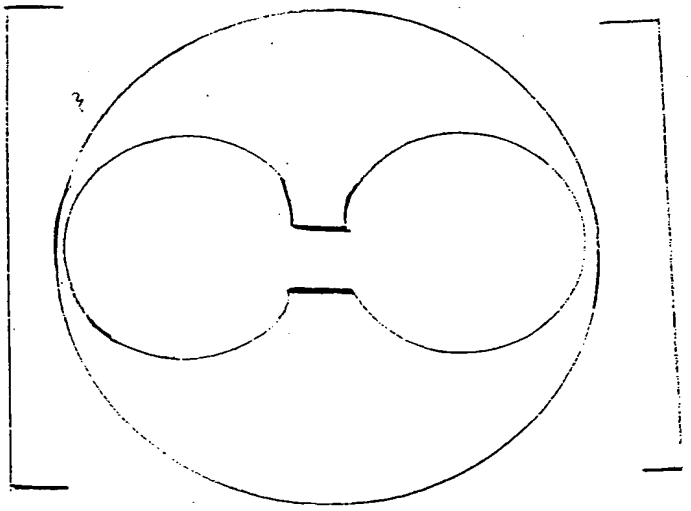


FIG. 47A

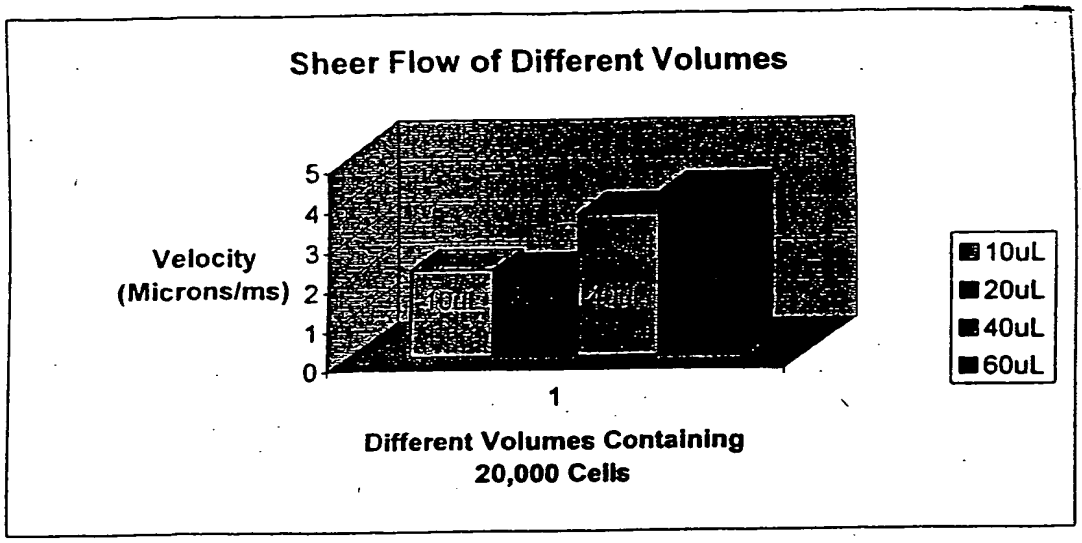

Sheer Flow of Different Volumes
Velocity (Microns/ms)
5
4
3
2
1
0
1
Different Volumes Containing 20,000 Cells
10uL
20uL
40uL
60uL

FIG. 48

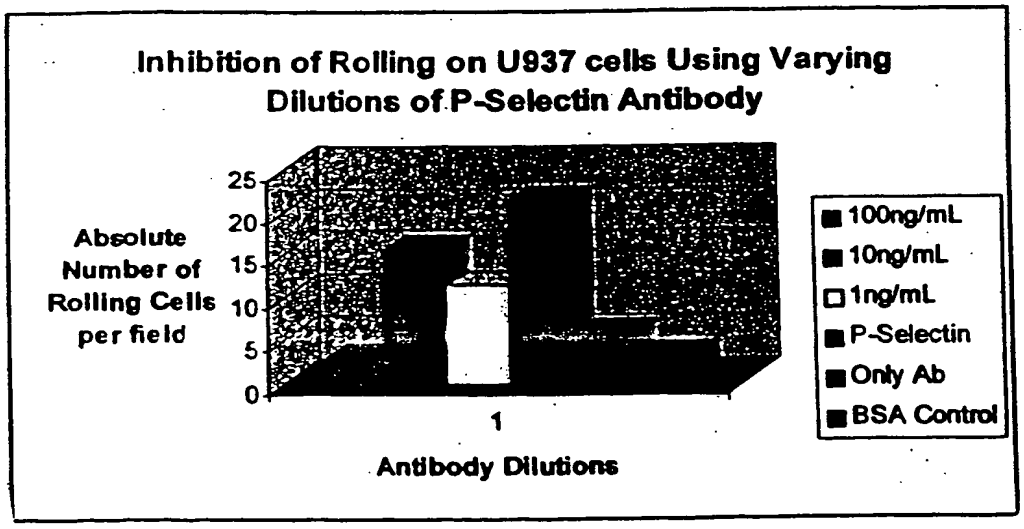
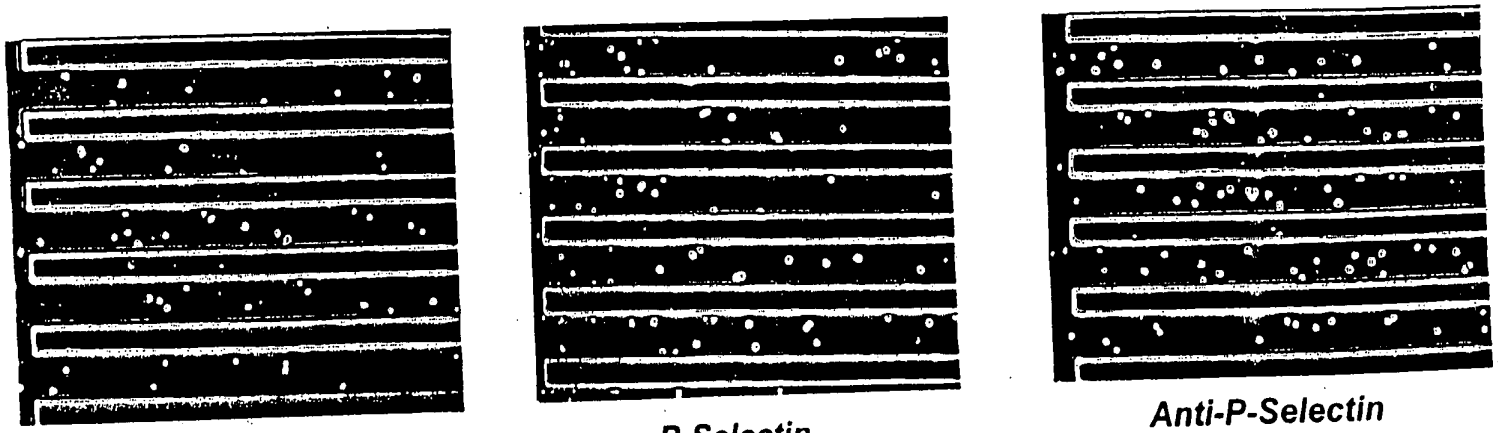

Inhibition of Rolling on U937 cells Using Varying Dilutions of P-Selectin Antibody
Absolute Number of Rolling Cells per field
25
20
15
10
5
0
1
Antibody Dilutions
100ng/mL
10ng/mL
1ng/mL
P-Selectin
Only Ab
BSA Control

FIG. 49

Monocytic cell line (THP-1) rolling and adhering to P-selectin



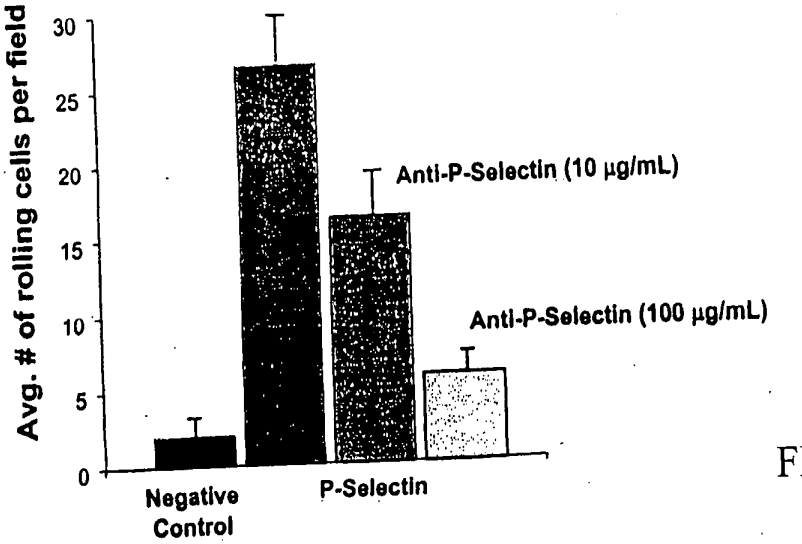
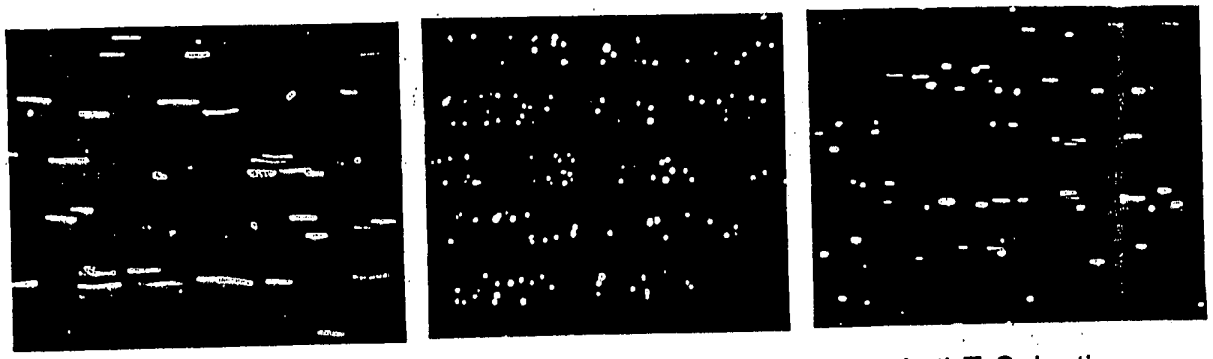


FIG. 50


Negative Control
E-Selectin: Rolling Cells
Anti-E-Selectin

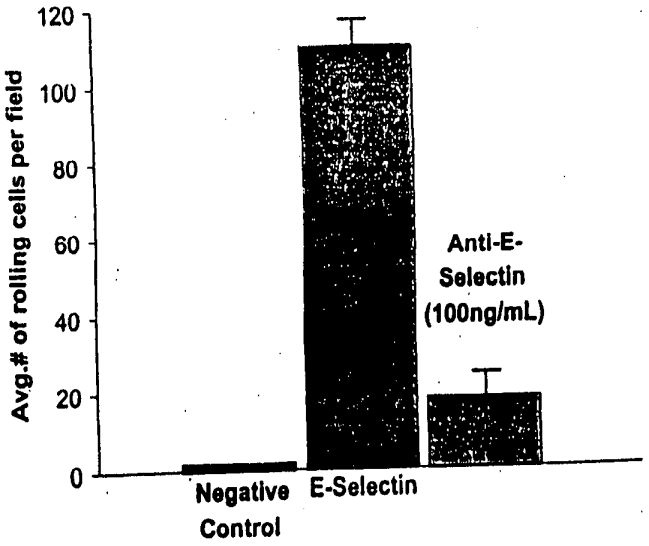

120
100
80
60
40
20
0
Avg.# of rolling cells per field
Anti-E-Selectin (100ng/mL)
Negative Control
E-Selectin

FIG. 51

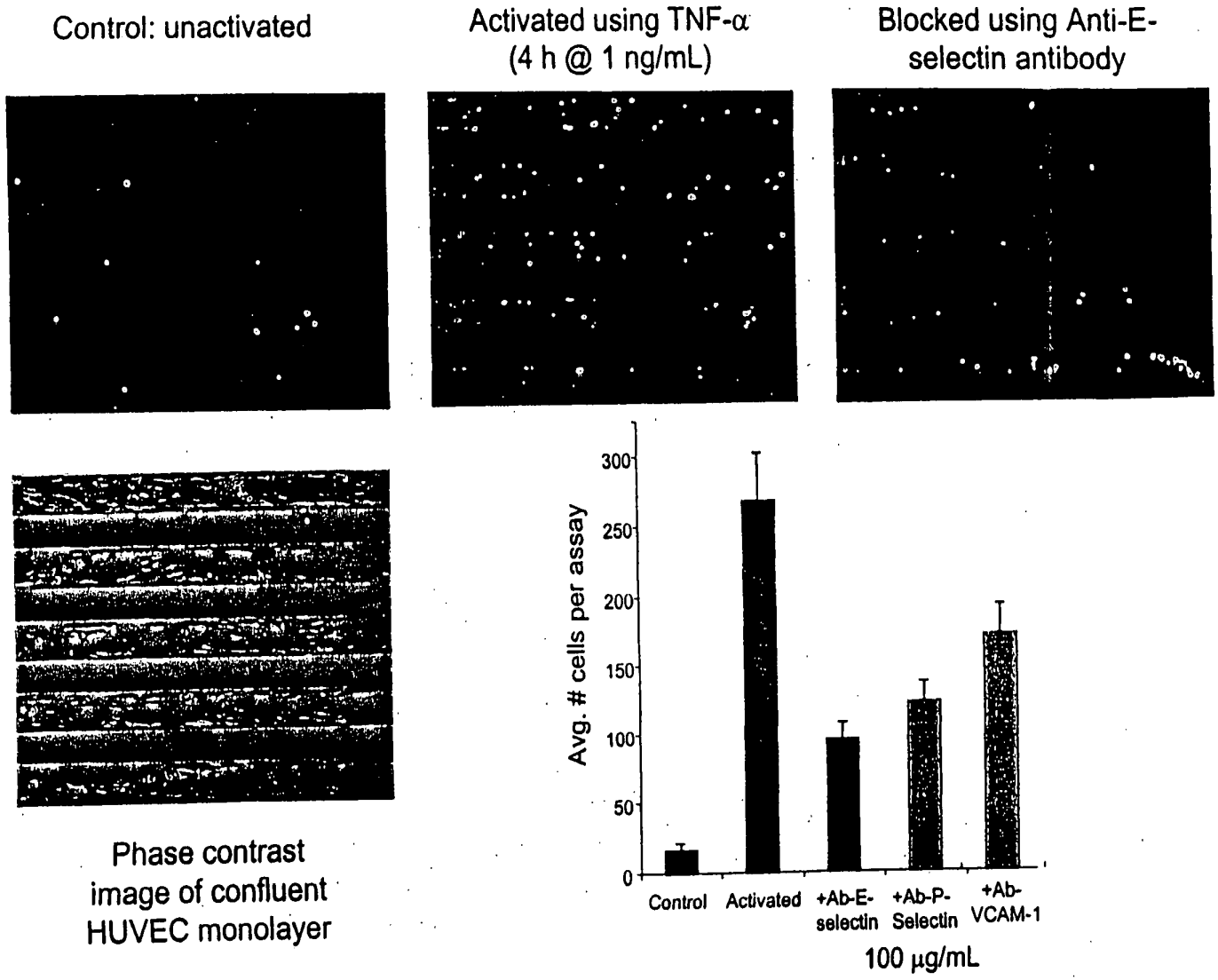

Control: unactivated
Activated using TNF-α (4 h @ 1 ng/mL)
Blocked using Anti-E-selectin antibody
Phase contrast image of confluent HUVEC monolayer
Avg. # cells per assay
300
250
200
150
100
50
0
Control
Activated
+Ab-E-selectin
+Ab-P-Selectin
+Ab-VCAM-1
100 µg/mL

FIG. 52

Selective Activation of Endothelium

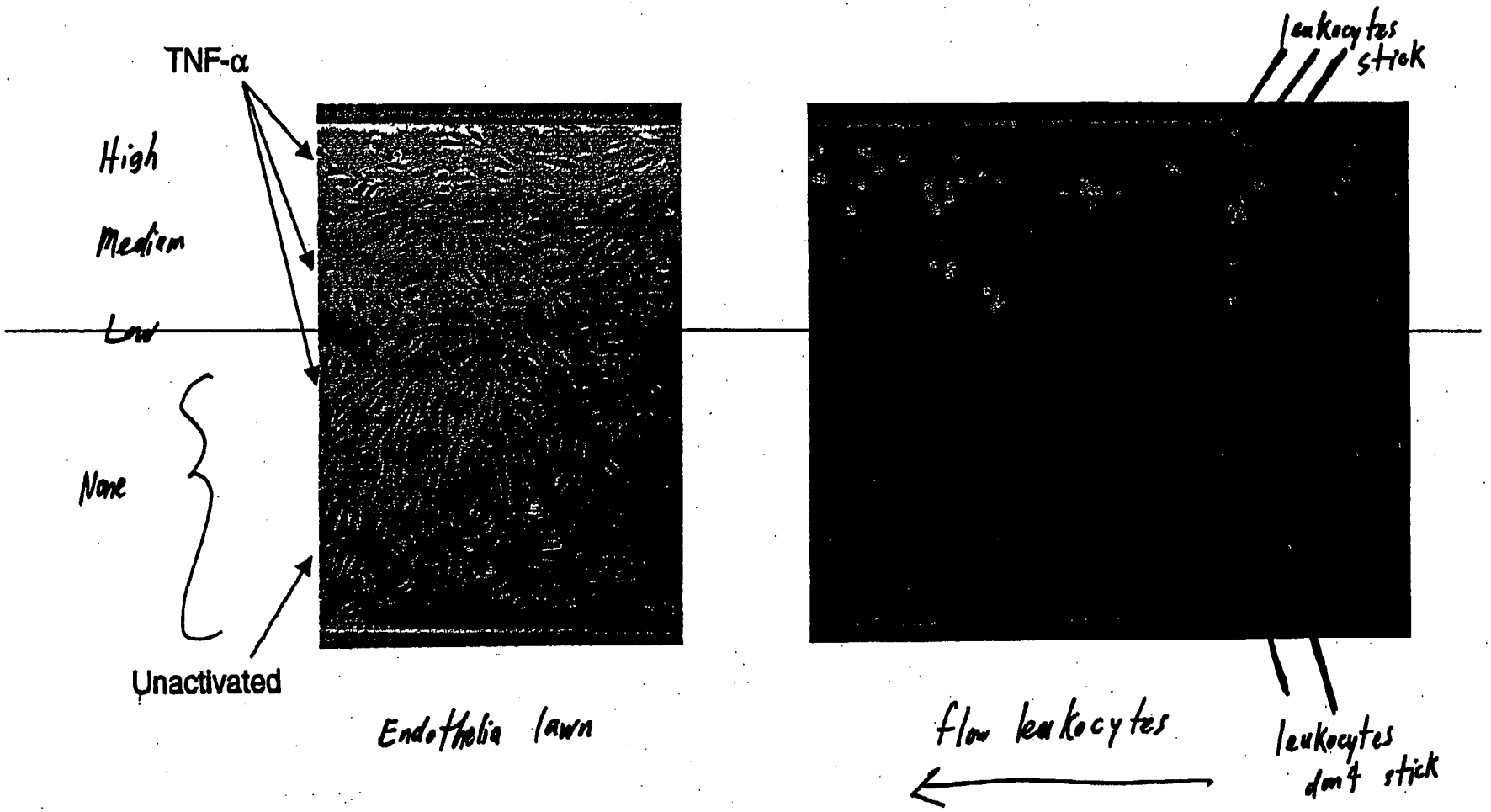


FIG. 53

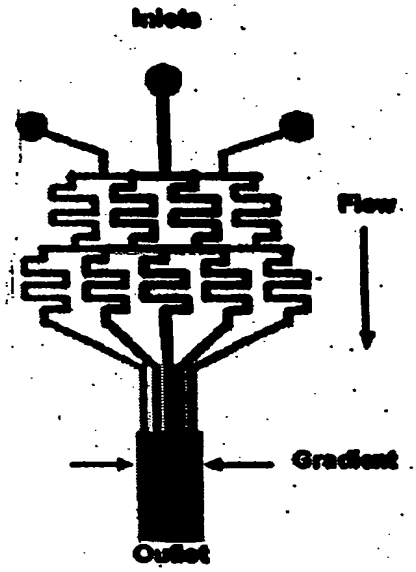


FIG. 54

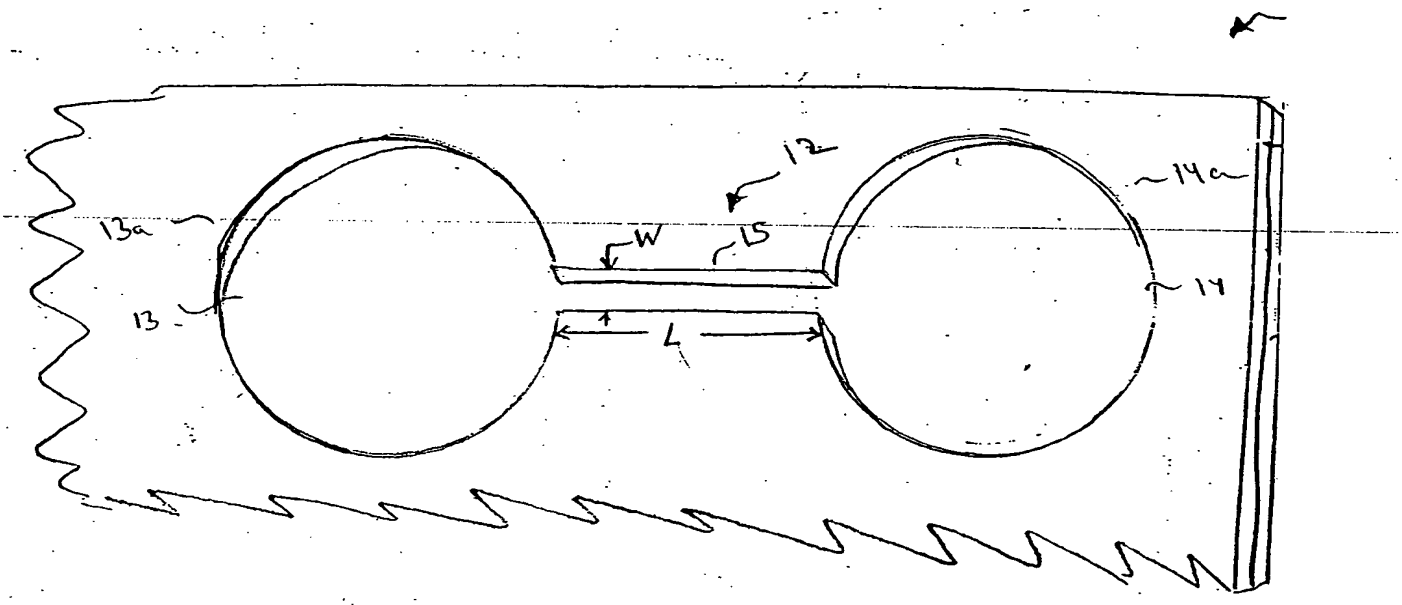


FIG. 55A

FIG. 55B

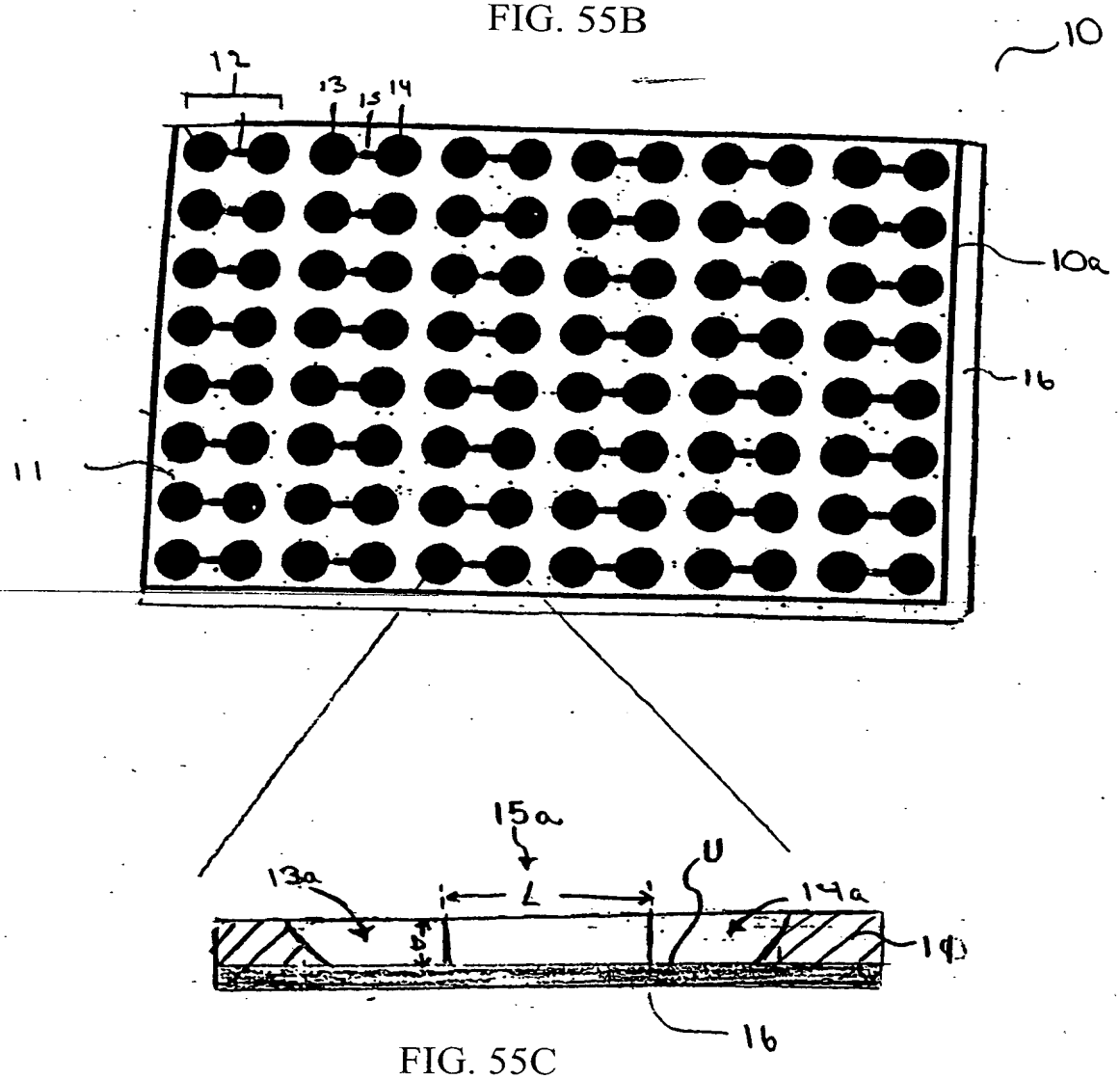


FIG. 55C

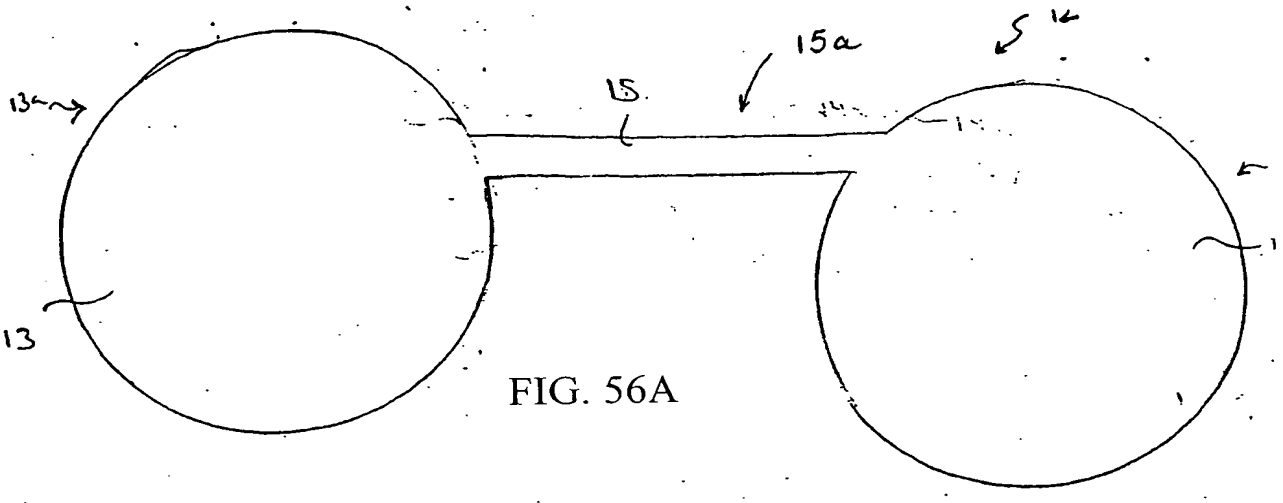


FIG. 56A

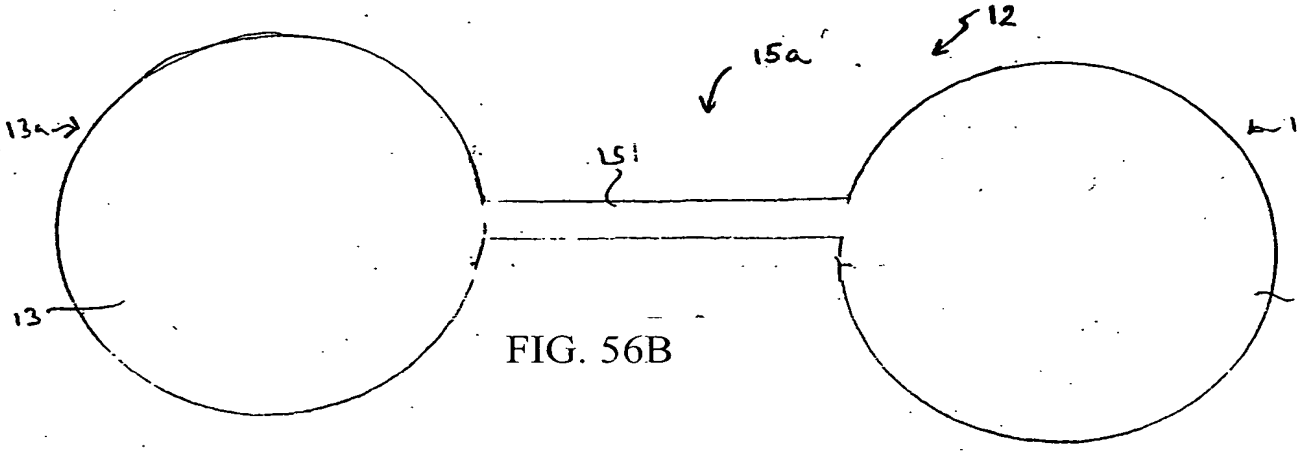


FIG. 56B

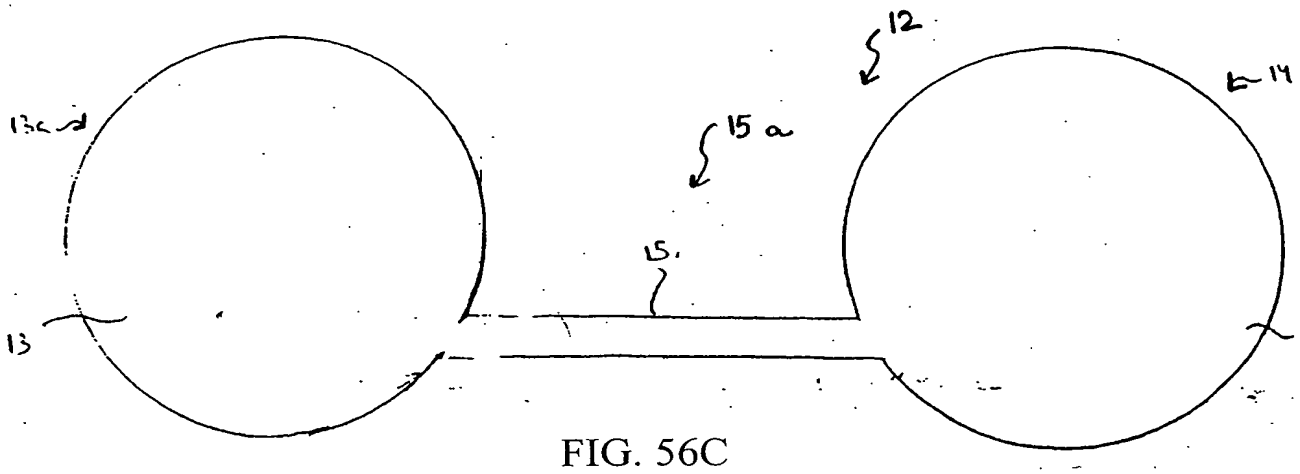


FIG. 56C

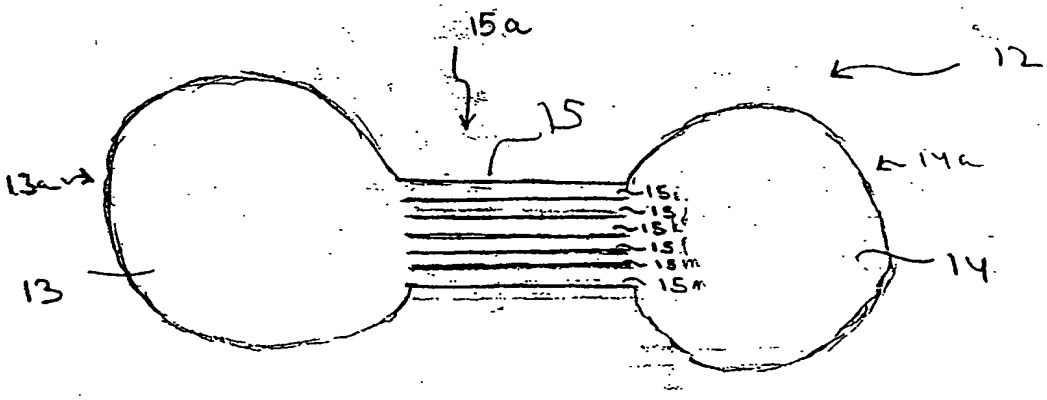


FIG. 57A

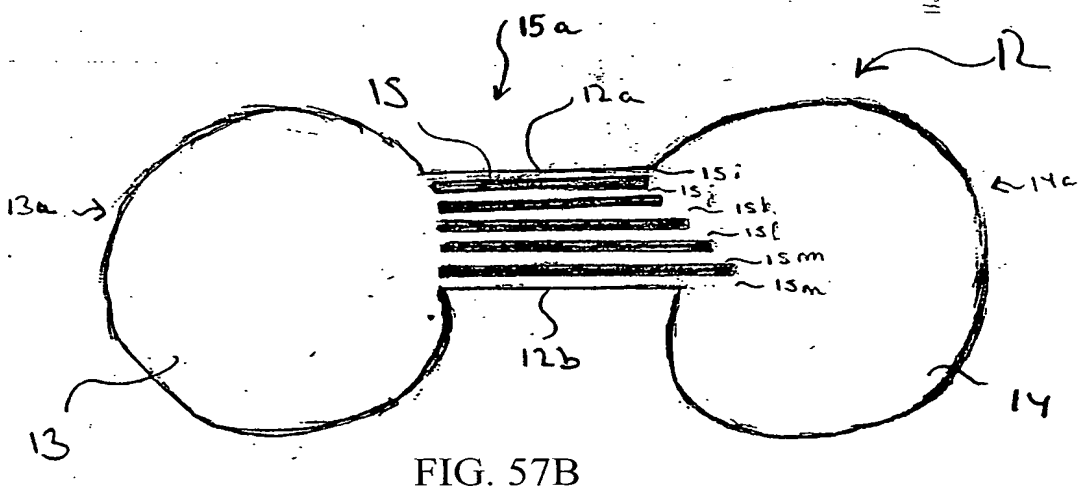


FIG. 57B

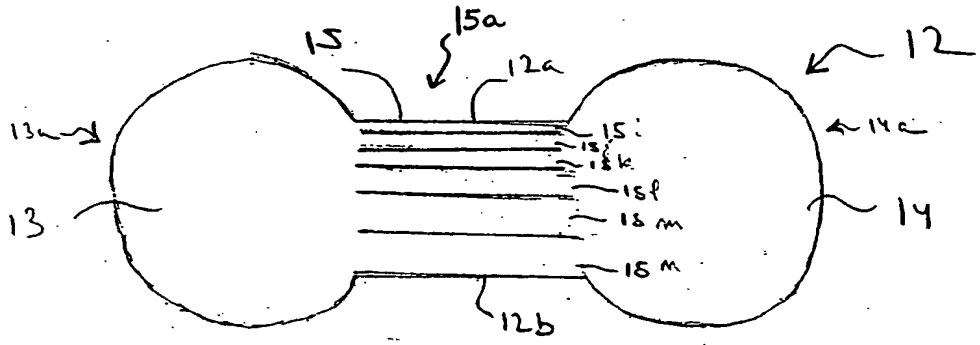


FIG. 57C

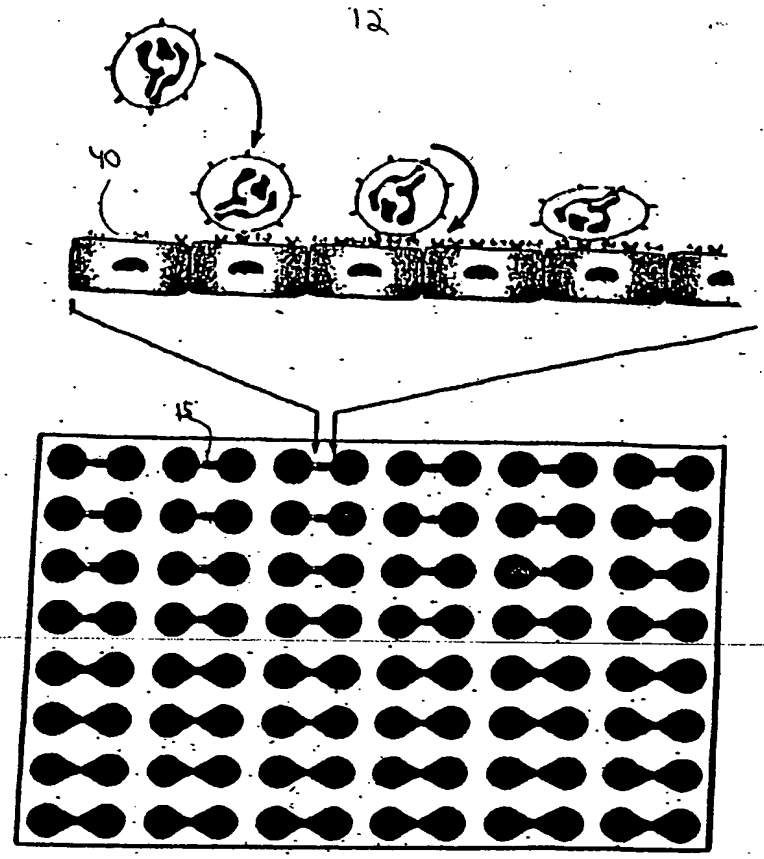


FIG. 58B

FIG. 58A

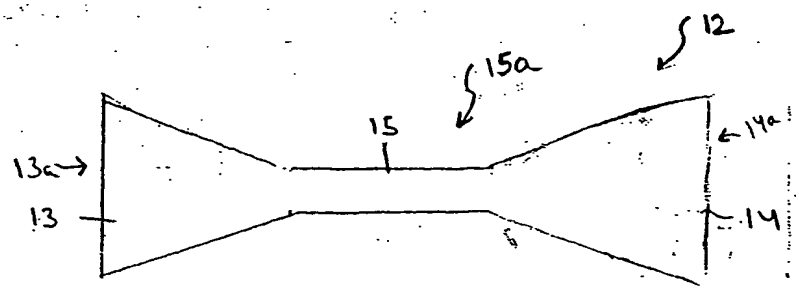


FIG. 59

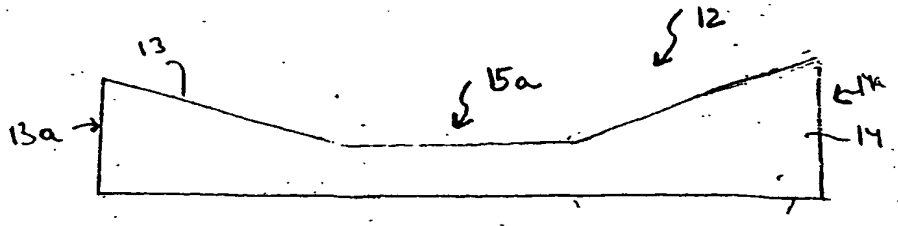


FIG. 60

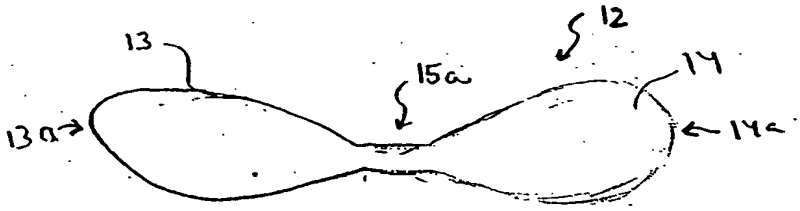


FIG. 61

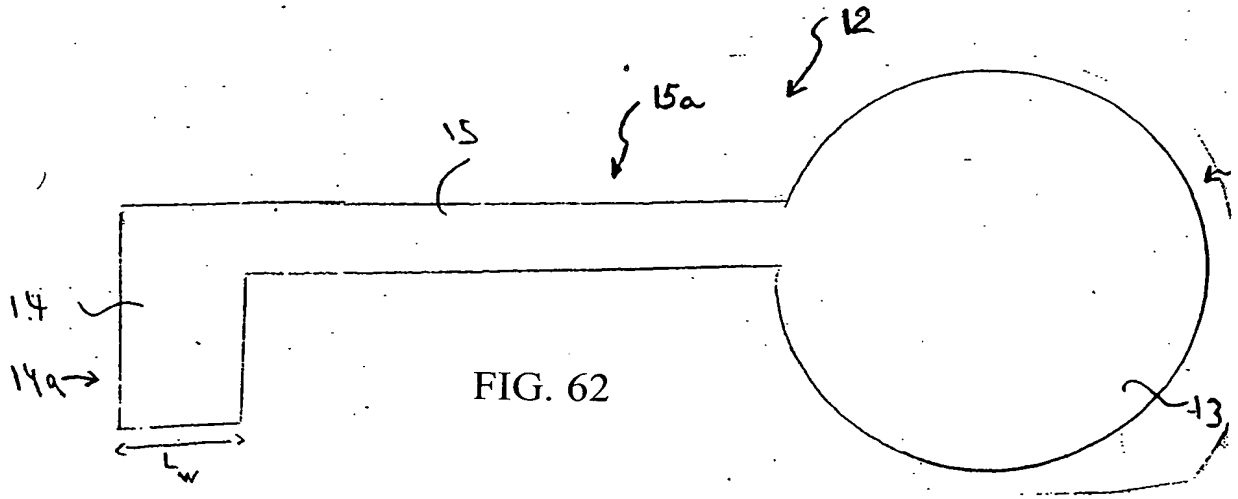


FIG. 62

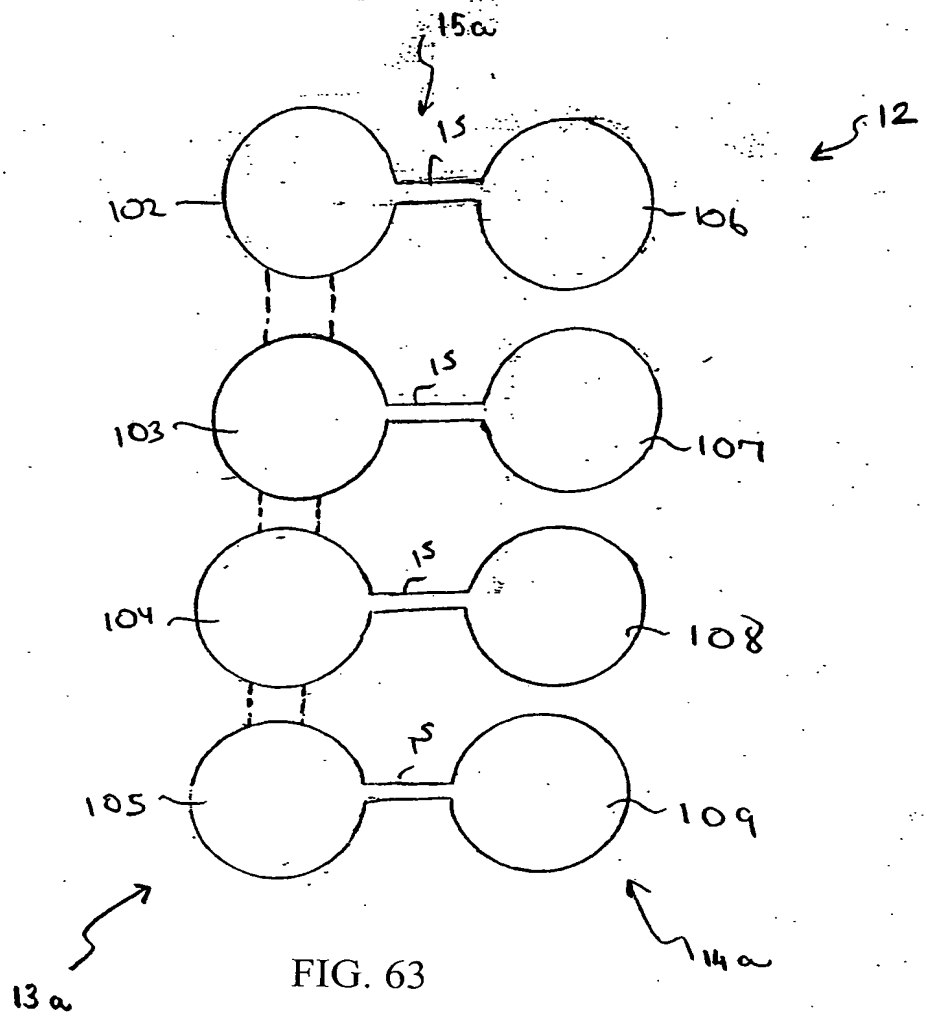


FIG. 63

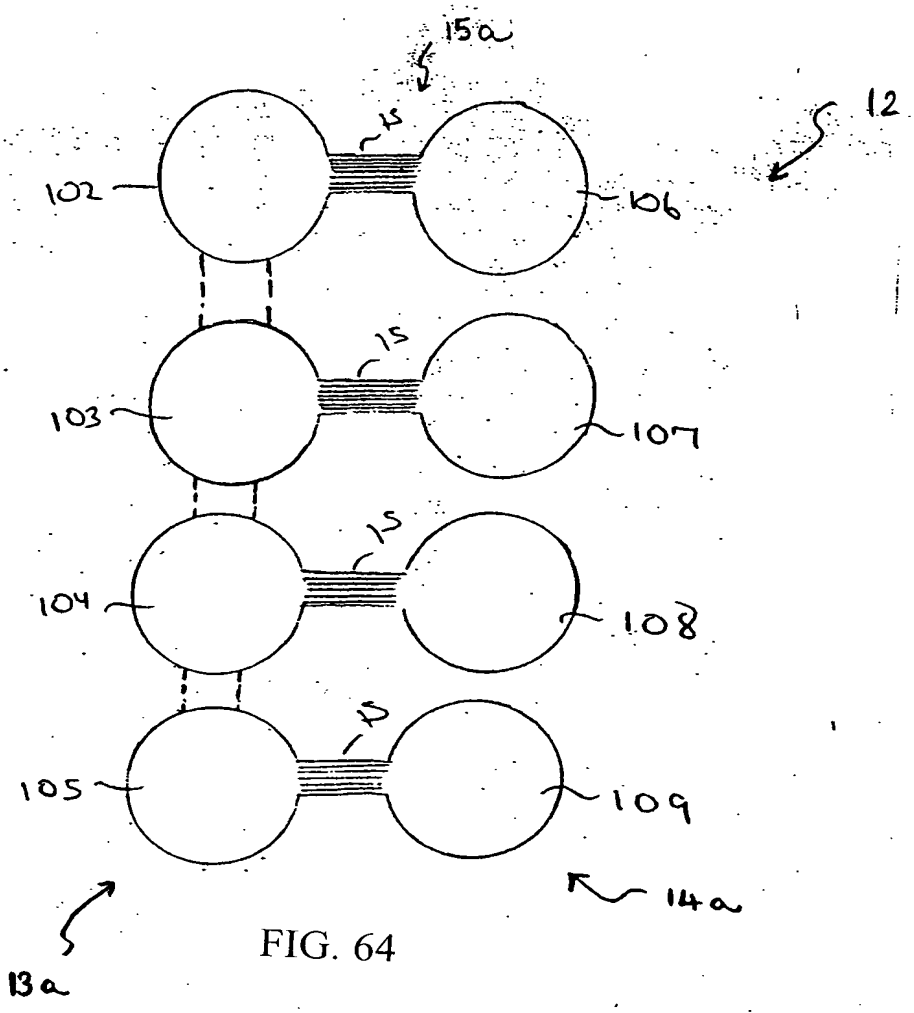


FIG. 64

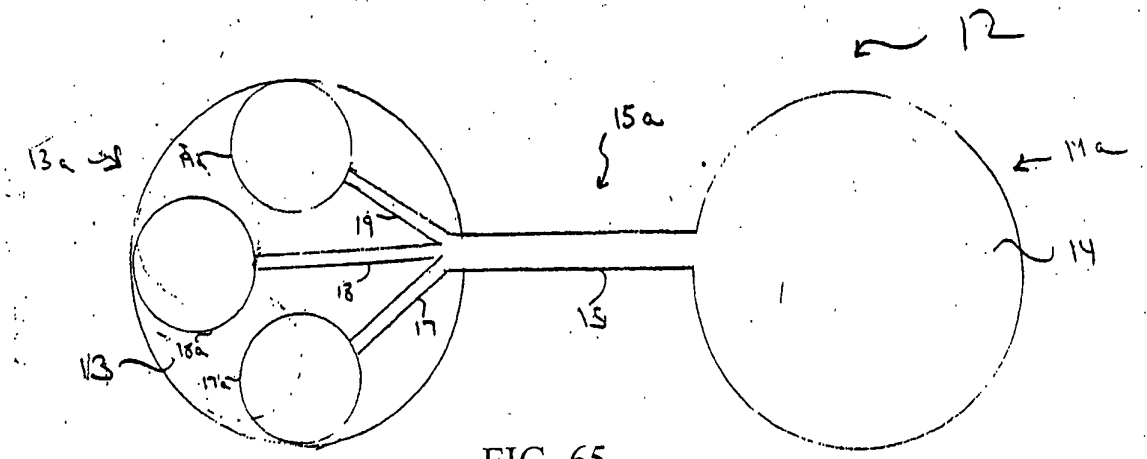


FIG. 65

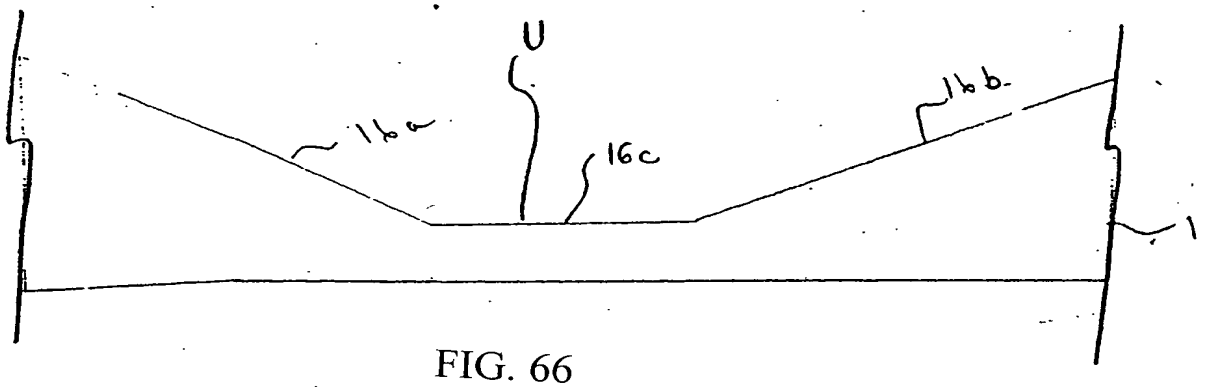


FIG. 66

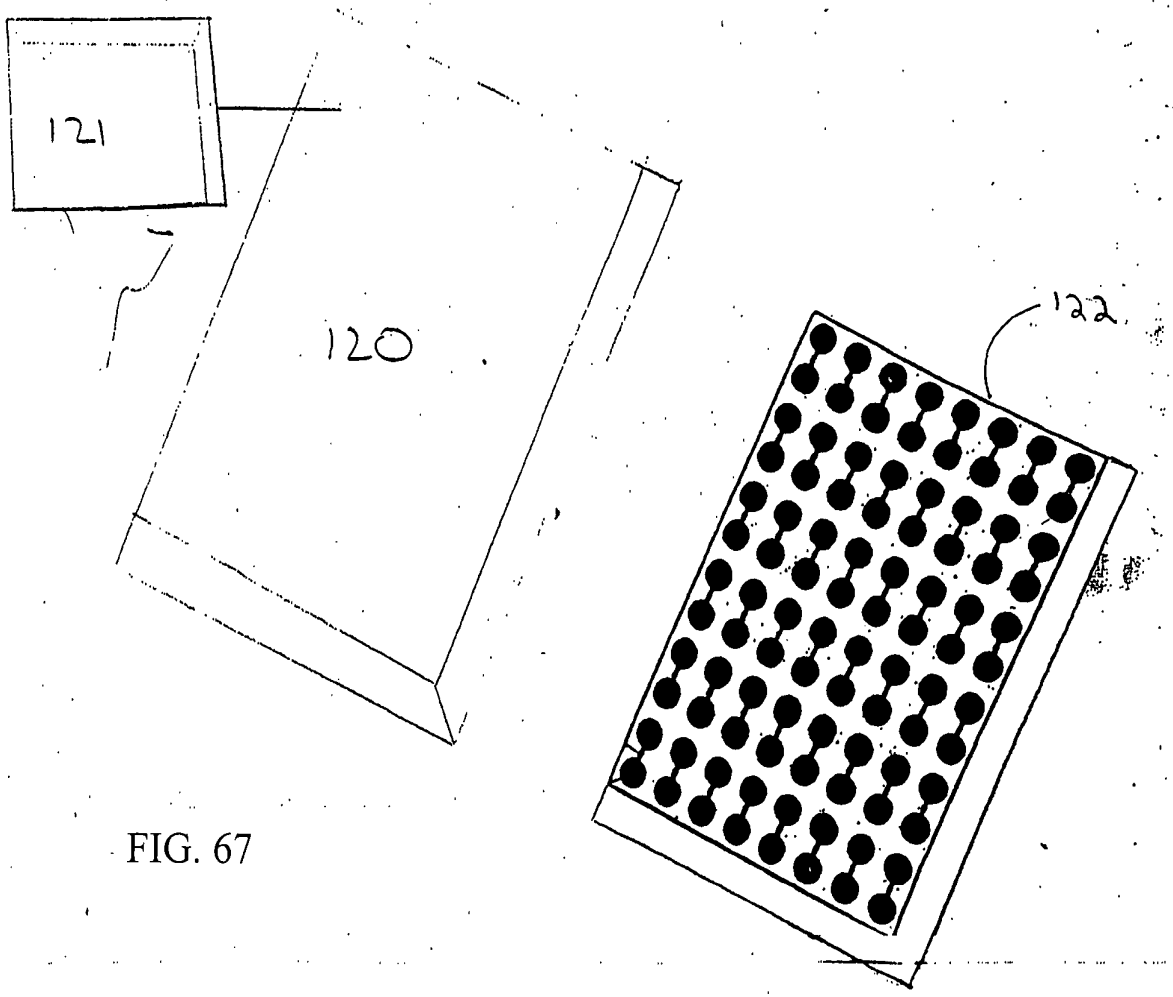


FIG. 67

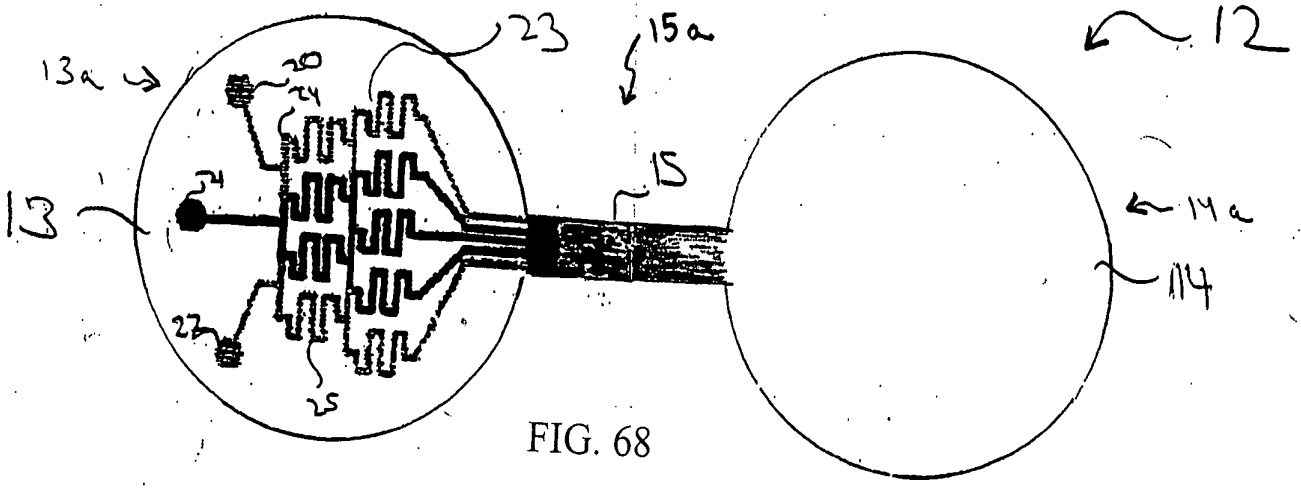


FIG. 68

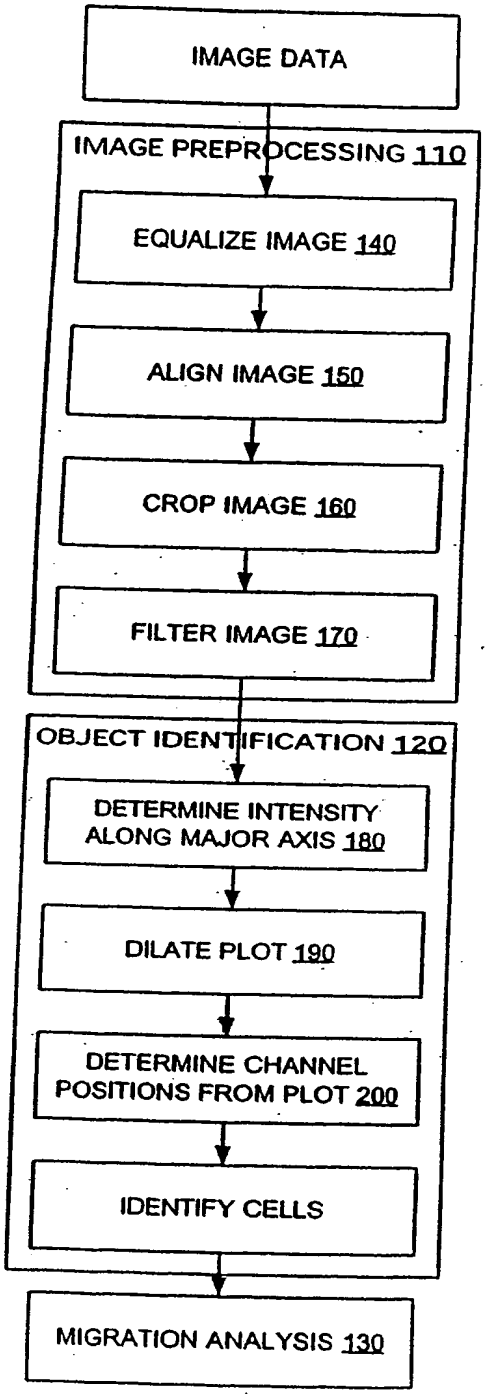


IMAGE DATA
IMAGE PREPROCESSING 110
EQUALIZE IMAGE 140
ALIGN IMAGE 150
CROP IMAGE 160
FILTER IMAGE 170
OBJECT IDENTIFICATION 120
DETERMINE INTENSITY ALONG MAJOR AXIS 180
DILATE PLOT 190
DETERMINE CHANNEL POSITIONS FROM PLOT 200
IDENTIFY CELLS
MIGRATION ANALYSIS 130

FIG. 69

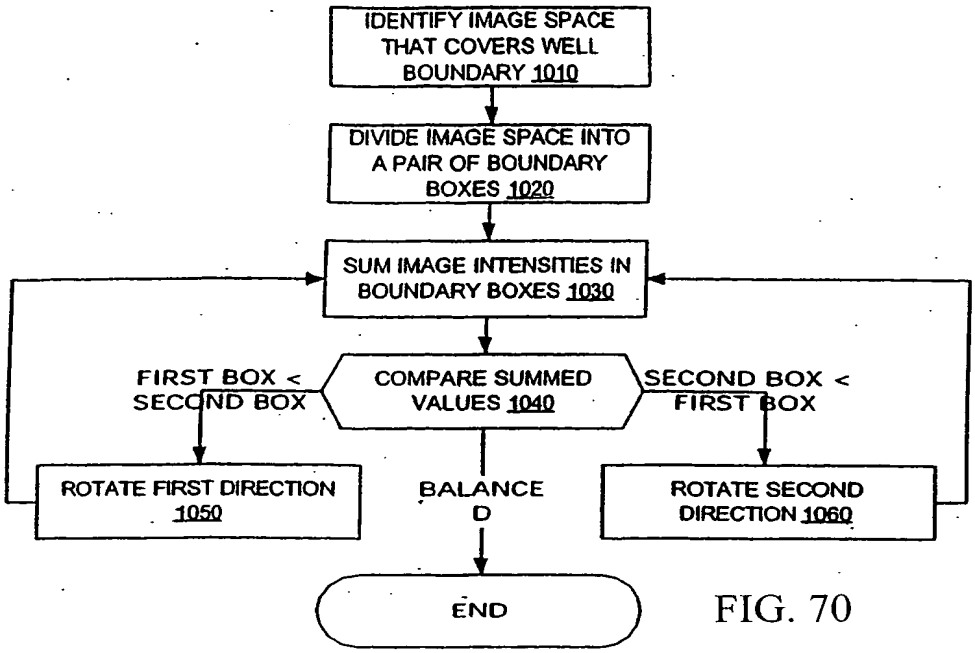
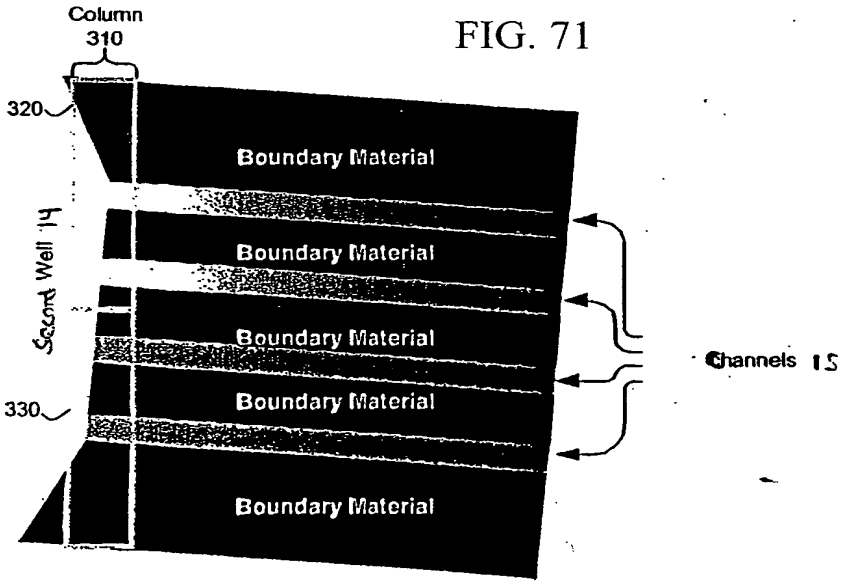

IDENTIFY IMAGE SPACE THAT COVERS WELL BOUNDARY 1010
DIVIDE IMAGE SPACE INTO A PAIR OF BOUNDARY BOXES 1020
SUM IMAGE INTENSITIES IN BOUNDARY BOXES 1030
FIRST BOX < SECOND BOX
COMPARE SUMMED VALUES 1040
SECOND BOX < FIRST BOX
ROTATE FIRST DIRECTION 1050
BALANCED
ROTATE SECOND DIRECTION 1060
END

FIG. 70

FIG. 71


Column 310
320
Boundary Material
Boundary Material
Second Well 14
Boundary Material
Boundary Material
330
Boundary Material
Channels 15

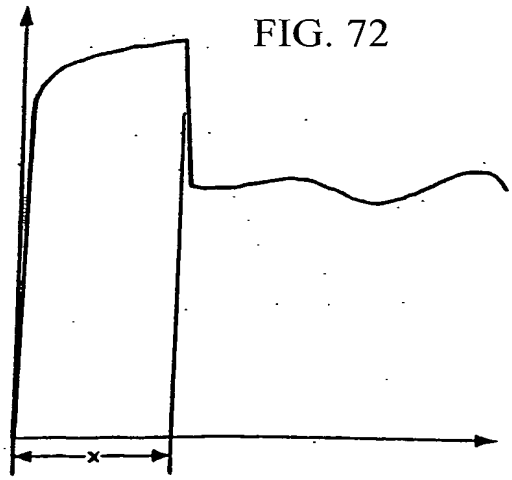


FIG. 72

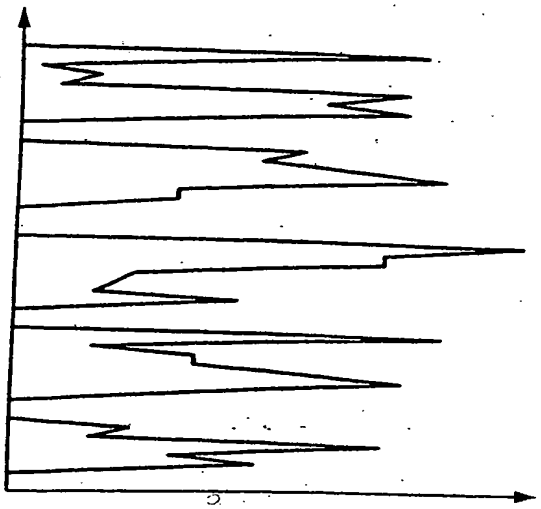
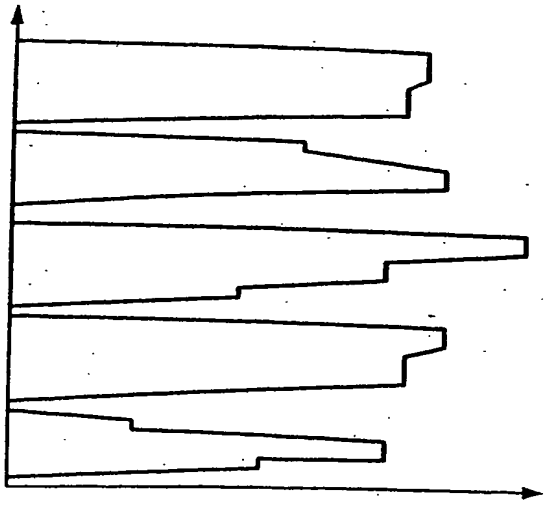
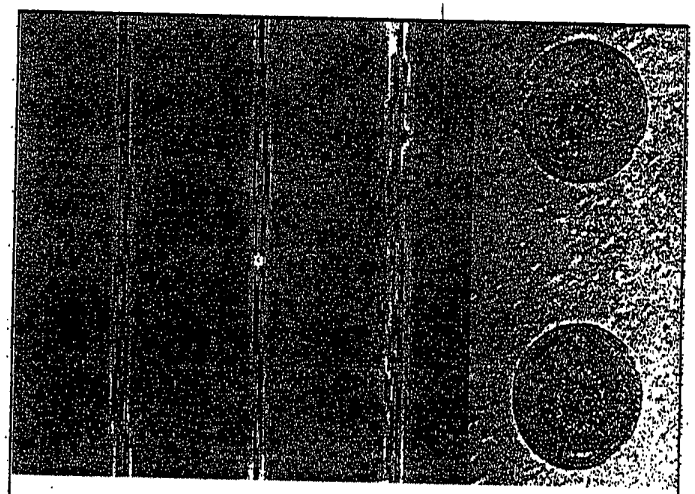


FIG. 73

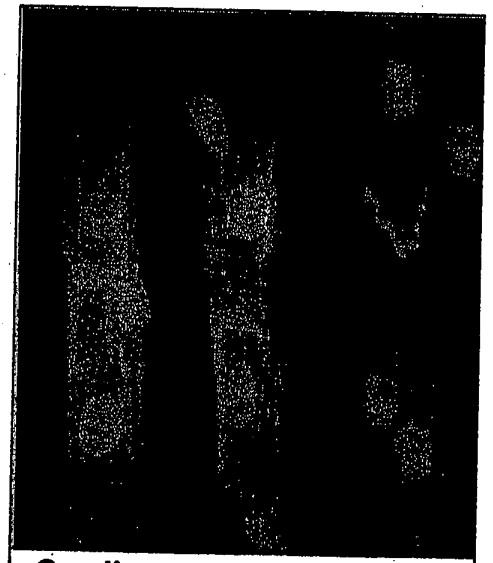
FIG. 74



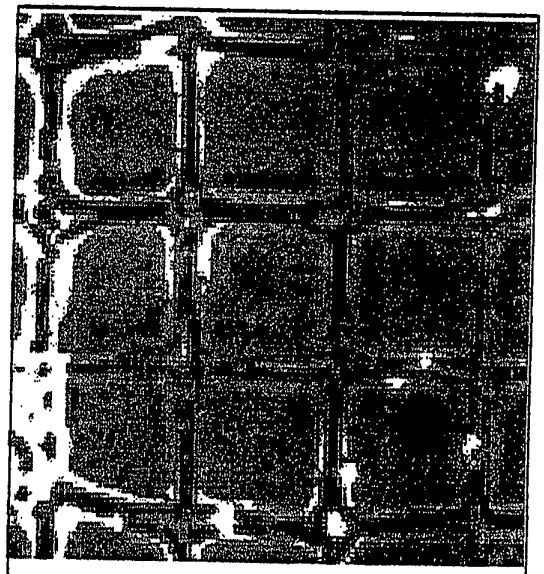
Hepatocytes- Bhatia



Endothelial Cells- Chen/Ostuni

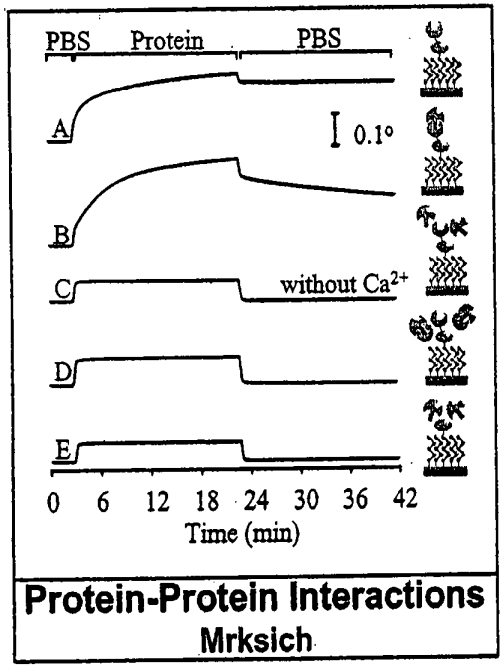


Cardiac myocytes-Stayton

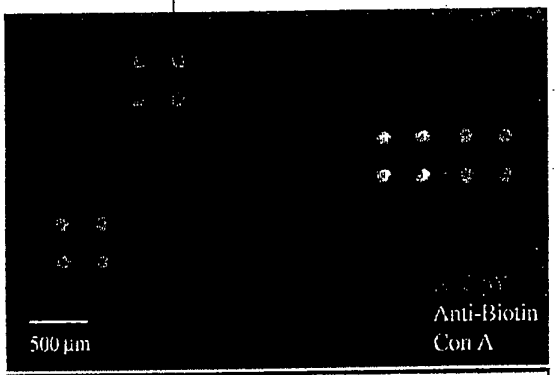


Neurons-Wheeler

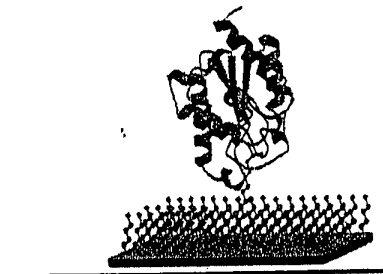
FIG. 75

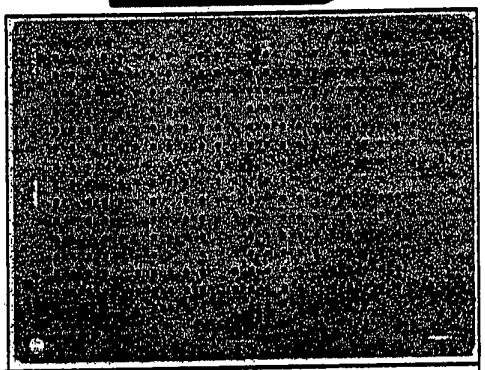


Protein-Protein Interactions
Mrksich

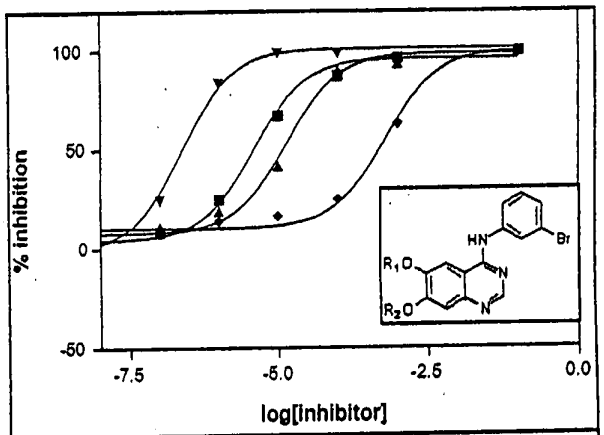


Patterned Ligands
Mrksich



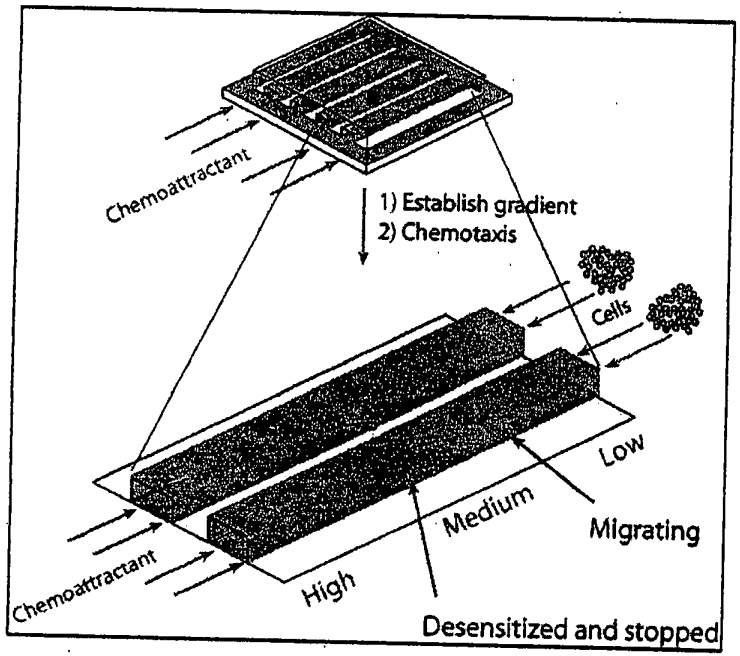


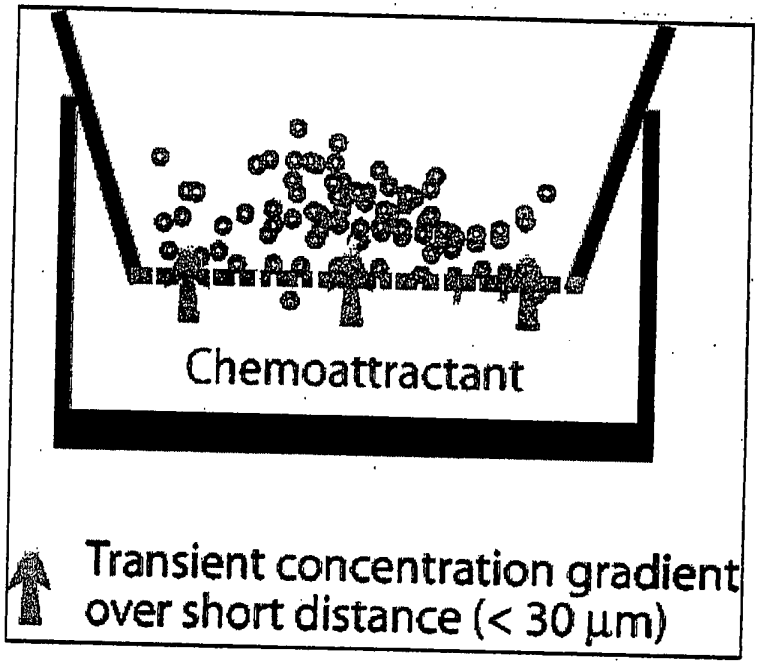
Kinase Substrate Fishing
Duffy



Kinase Inhibitor Screening
Duffy

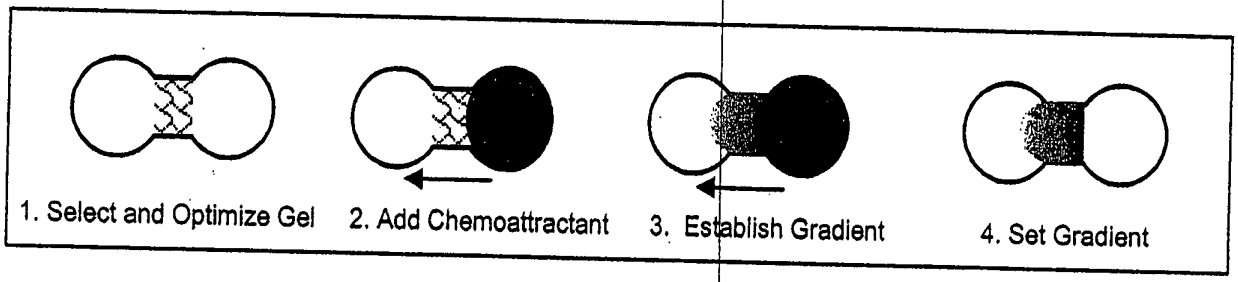
FIG. 76

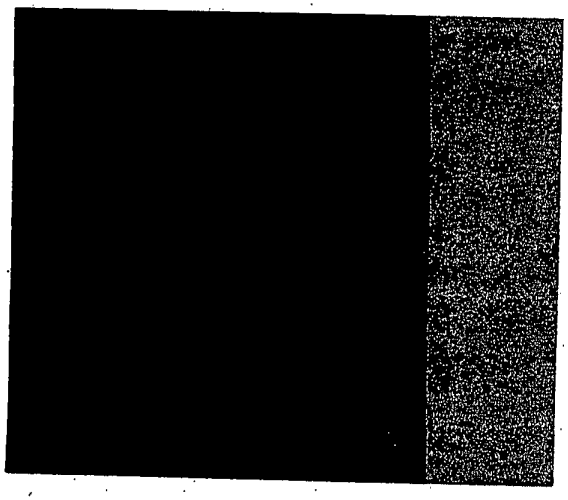




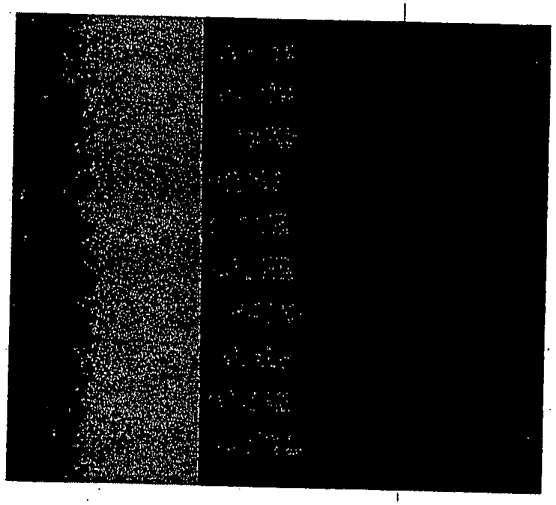
Surface Logix		Transwell
+	Stable chemical gradient	-
+	Linear chemical gradient	-
+	Gradient diversity (composition/size)	-
+	Quantifiable gradient	-
+	Real time monitoring	-
+	Distance traveled and density	-
+	Cell morphology	-

FIG. 77

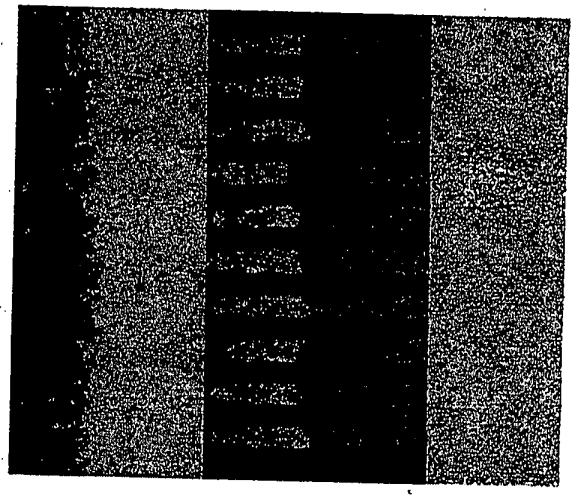




Gradient Formation
(MCP-1 + dye)



Migrating Cells (THP-1)



Robust Data

FIG. 78

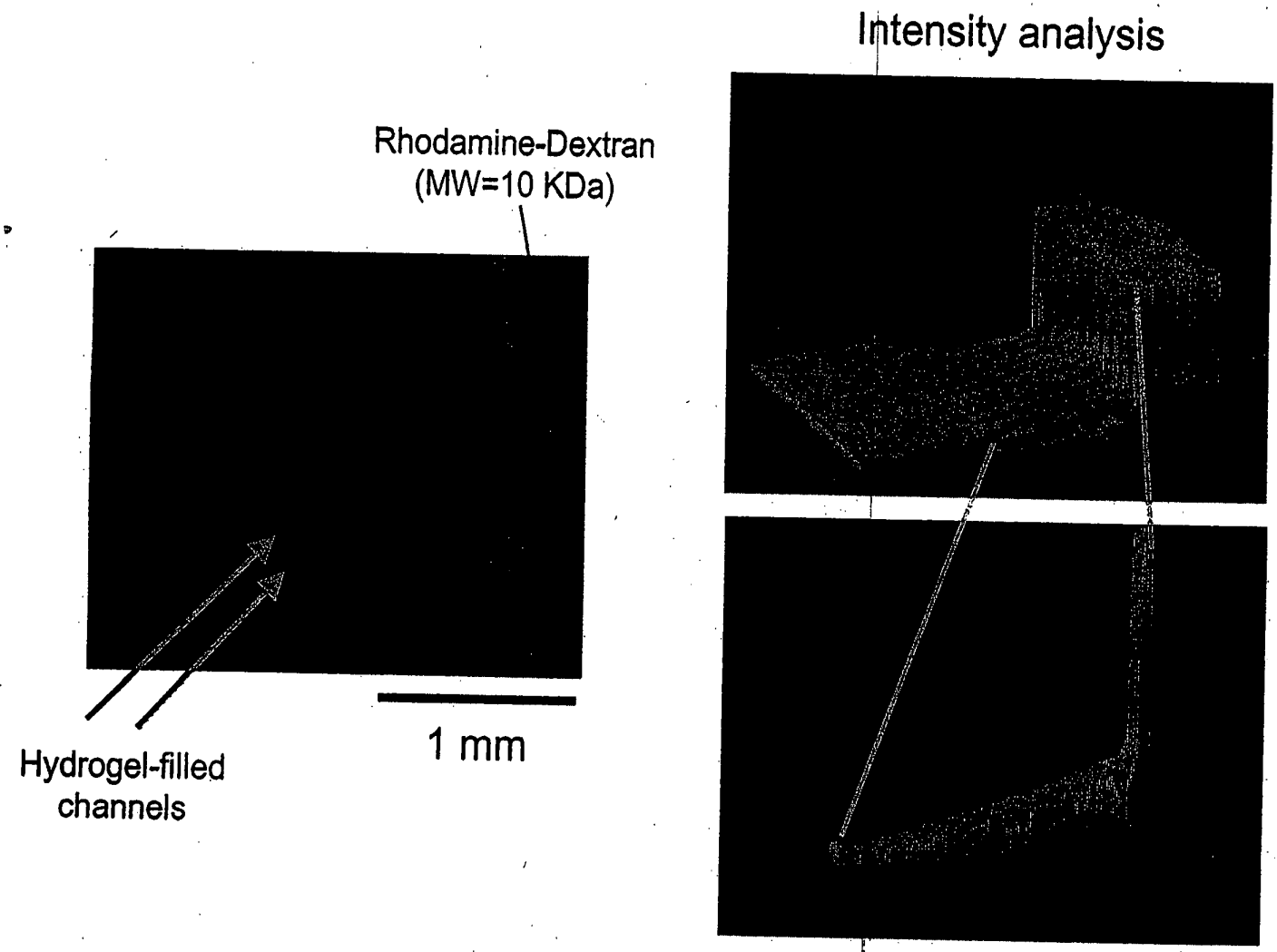

Intensity analysis
Rhodamine-Dextran
(MW=10 KDa)
1 mm
Hydrogel-filled
channels
Concentration at any point in the channel is calculated
from either linear or logarithmic best curve fit

FIG. 79

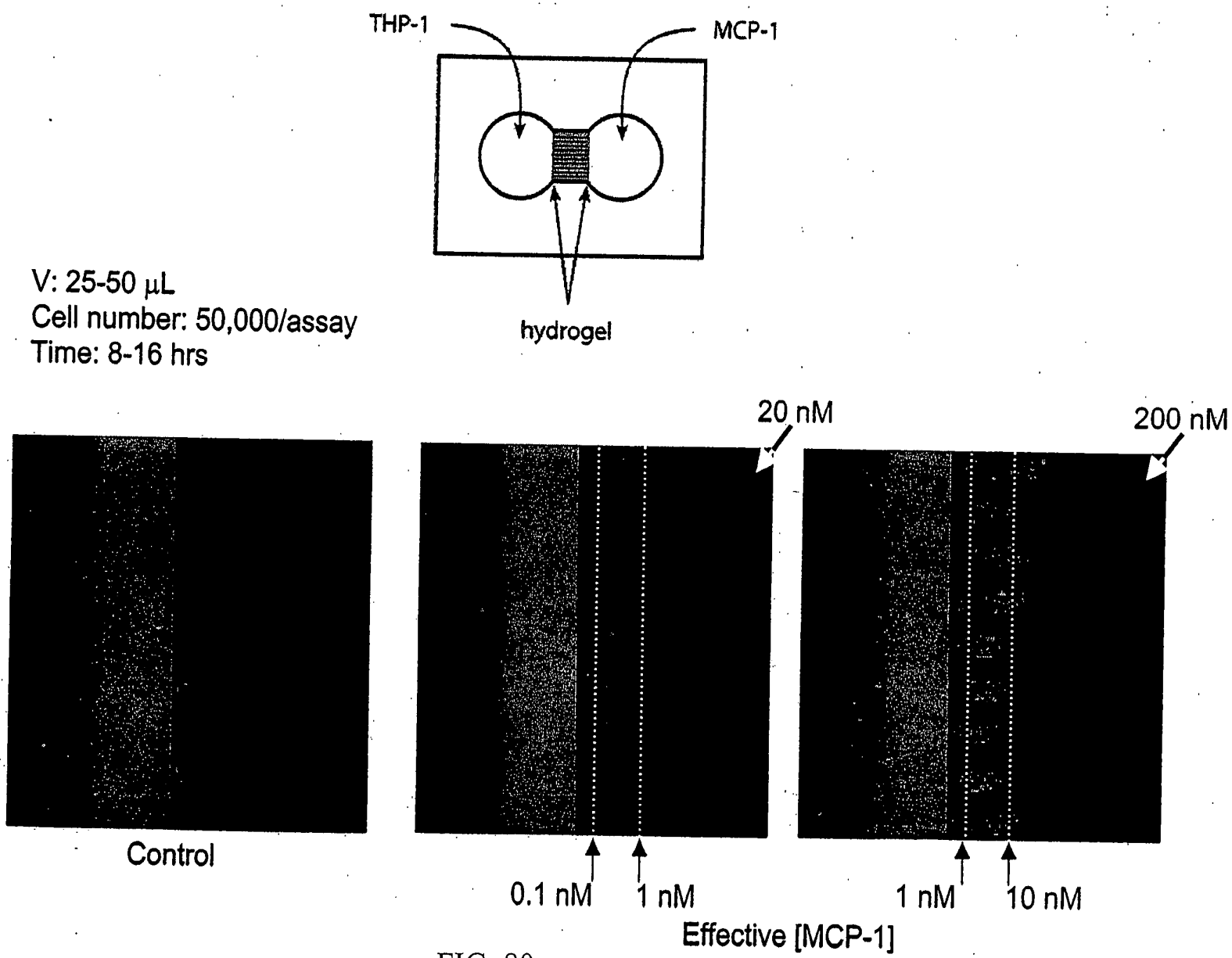

THP-1
MCP-1
hydrogel
V: 25-50 μL
Cell number: 50,000/assay
Time: 8-16 hrs
20 nM
200 nM
Control
0.1 nM
1 nM
1 nM
10 nM
Effective [MCP-1]

FIG. 80

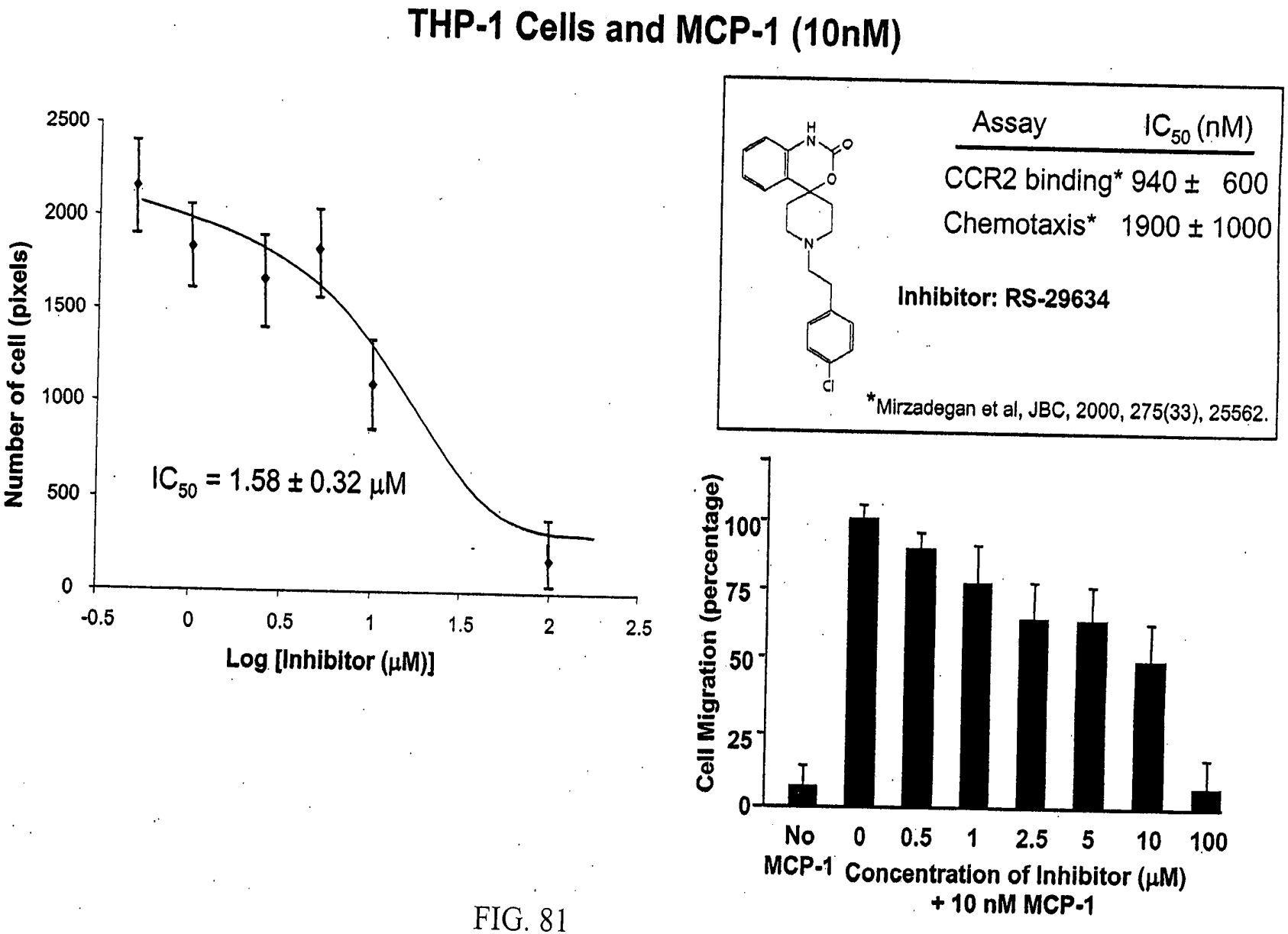
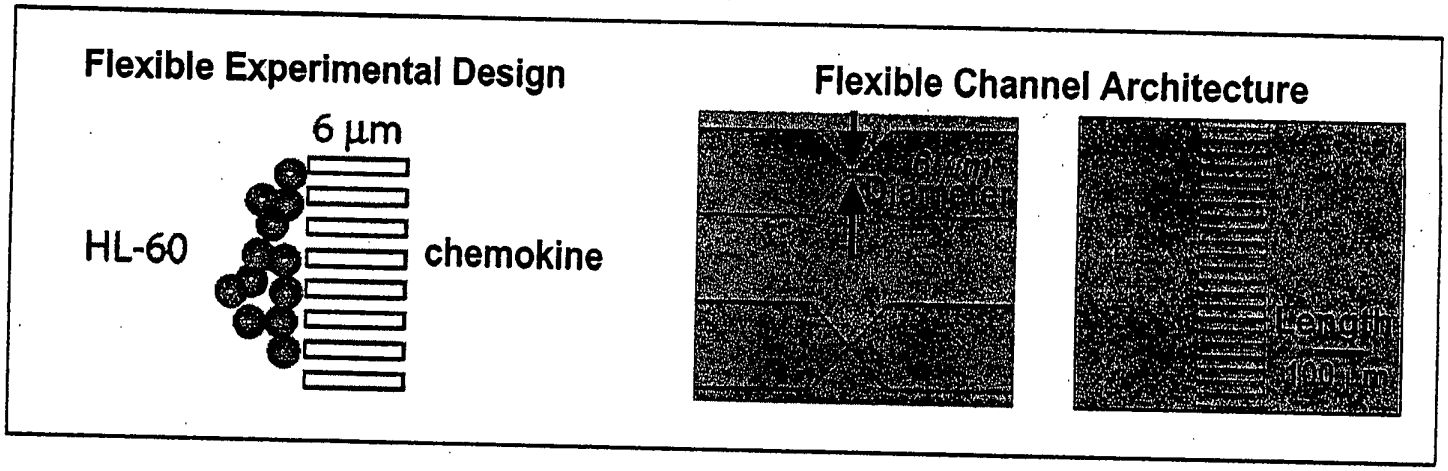

THP-1 Cells and MCP-1 (10nM)
Number of cell (pixels)
2500
2000
1500
1000
500
0
IC50 = 1.58 ± 0.32 µM
-0.5
0
0.5
1
1.5
2
2.5
Log [Inhibitor (µM)]
Assay
IC50 (nM)
CCR2 binding* 940 ± 600
Chemotaxis* 1900 ± 1000
Inhibitor: RS-29634
*Mirzadegan et al, JBC, 2000, 275(33), 25562.
Cell Migration (percentage)
100
75
50
25
0
No MCP-1
0
0.5
1
2.5
5
10
100
Concentration of Inhibitor (µM) + 10 nM MCP-1

FIG. 81


Flexible Experimental Design
6 µm
HL-60
chemokine
Flexible Channel Architecture
6 µm Diameter
Length
100 µm

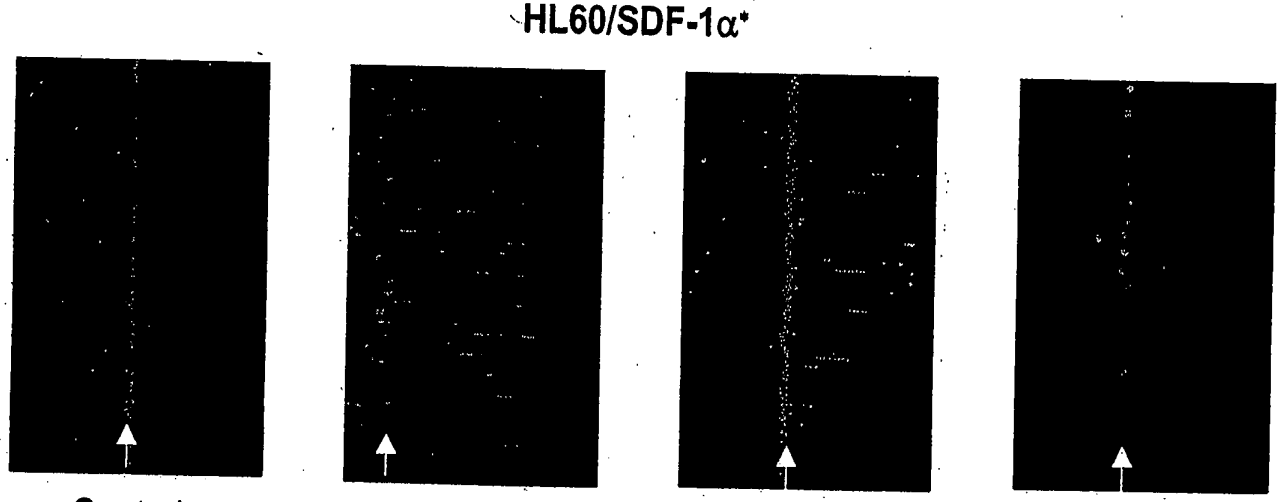
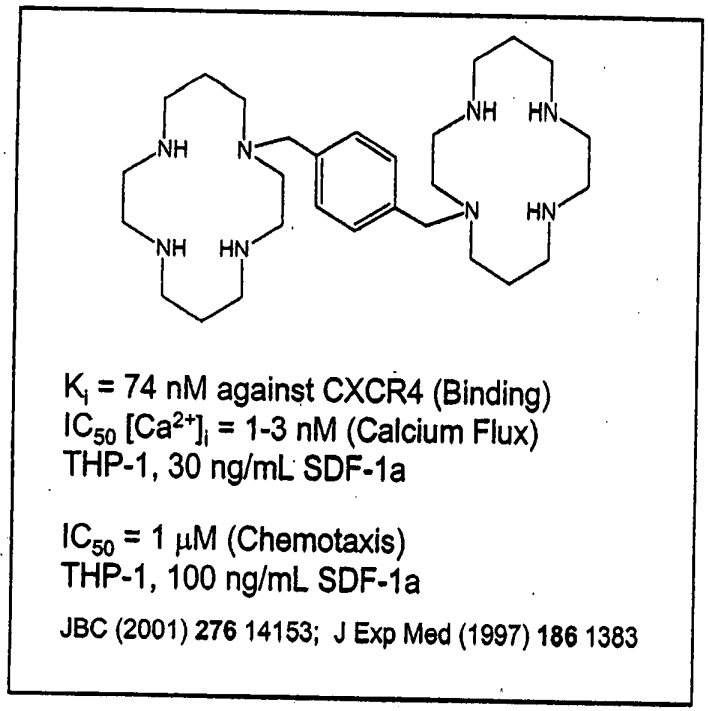

HL60/SDF-1α*
Control
2 nM SDF-1α
2 nM SDF-1α
100 nM AMD 3100
2 nM SDF-1α
1 µM AMD 3100
*30 minutes, 10,000 cells/assay,
preincubated inhibitors

FIG. 82

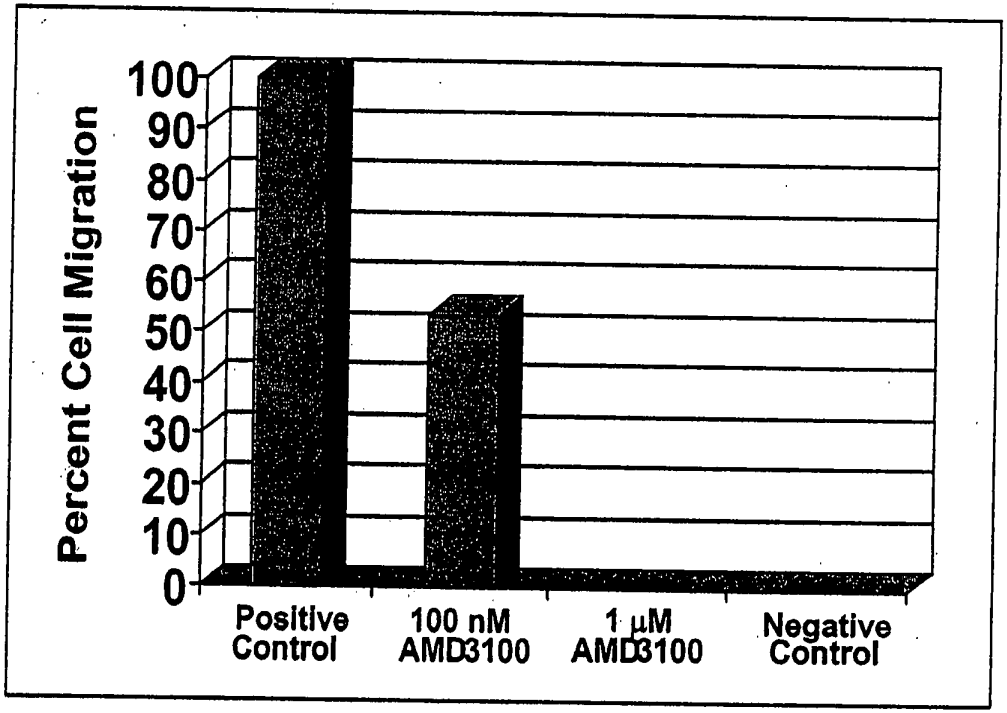


K_i = 74 nM against CXCR4 (Binding)
IC_{50} $[Ca^{2+}]_i$ = 1-3 nM (Calcium Flux)
THP-1, 30 ng/mL SDF-1a

IC_{50} = 1 μM (Chemotaxis)
THP-1, 100 ng/mL SDF-1a

JBC (2001) **276** 14153; J Exp Med (1997) **186** 1383

HL60/SDF-1α (2 nM, 30 minutes)



Proof of Principle Experiment (N=1 Cell Count Experiment)
Simplistic Data Analysis

FIG. 83

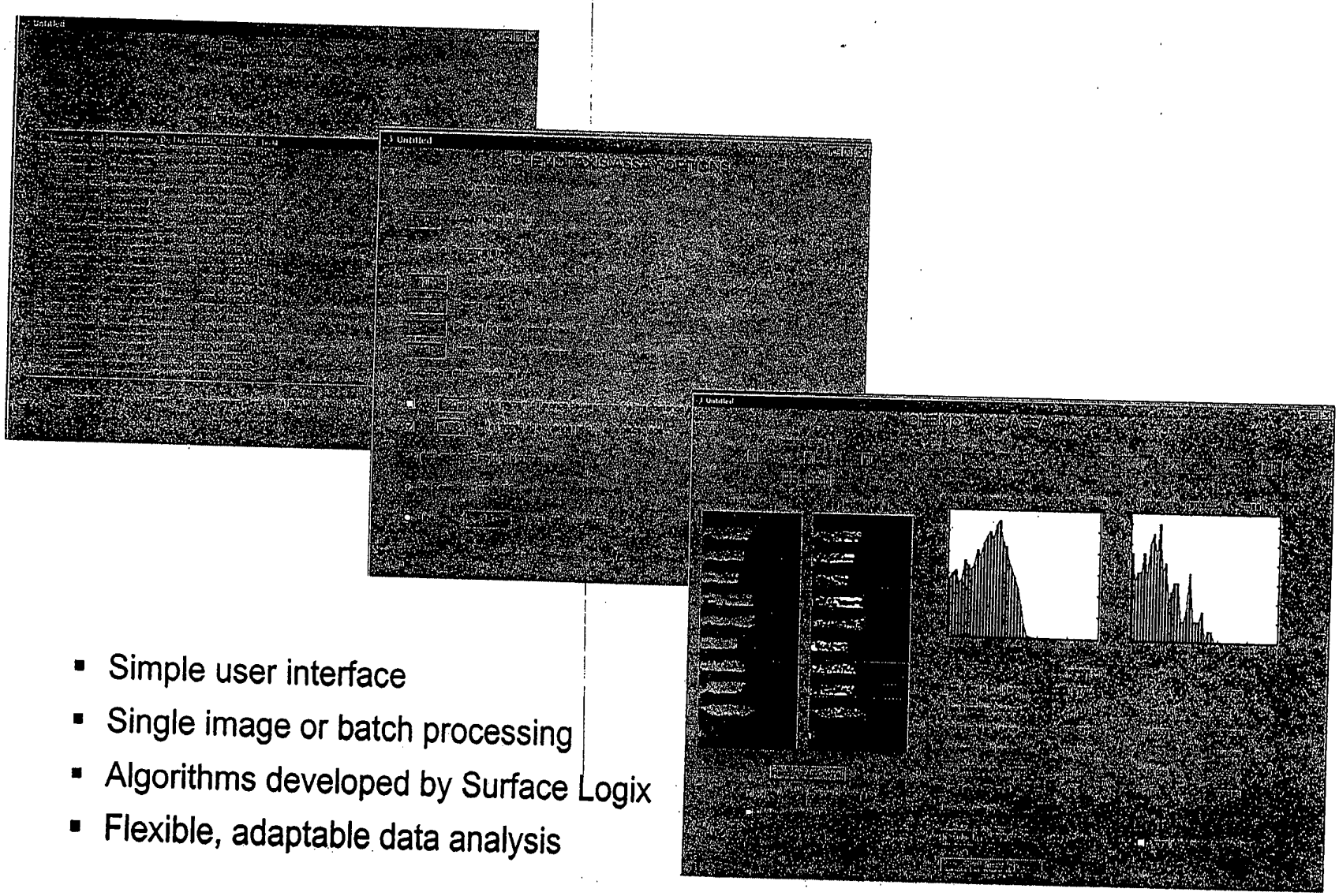

Simple user interface
Single image or batch processing
Algorithms developed by Surface Logix
Flexible, adaptable data analysis

FIG. 84

Selective Activation of Endothelium

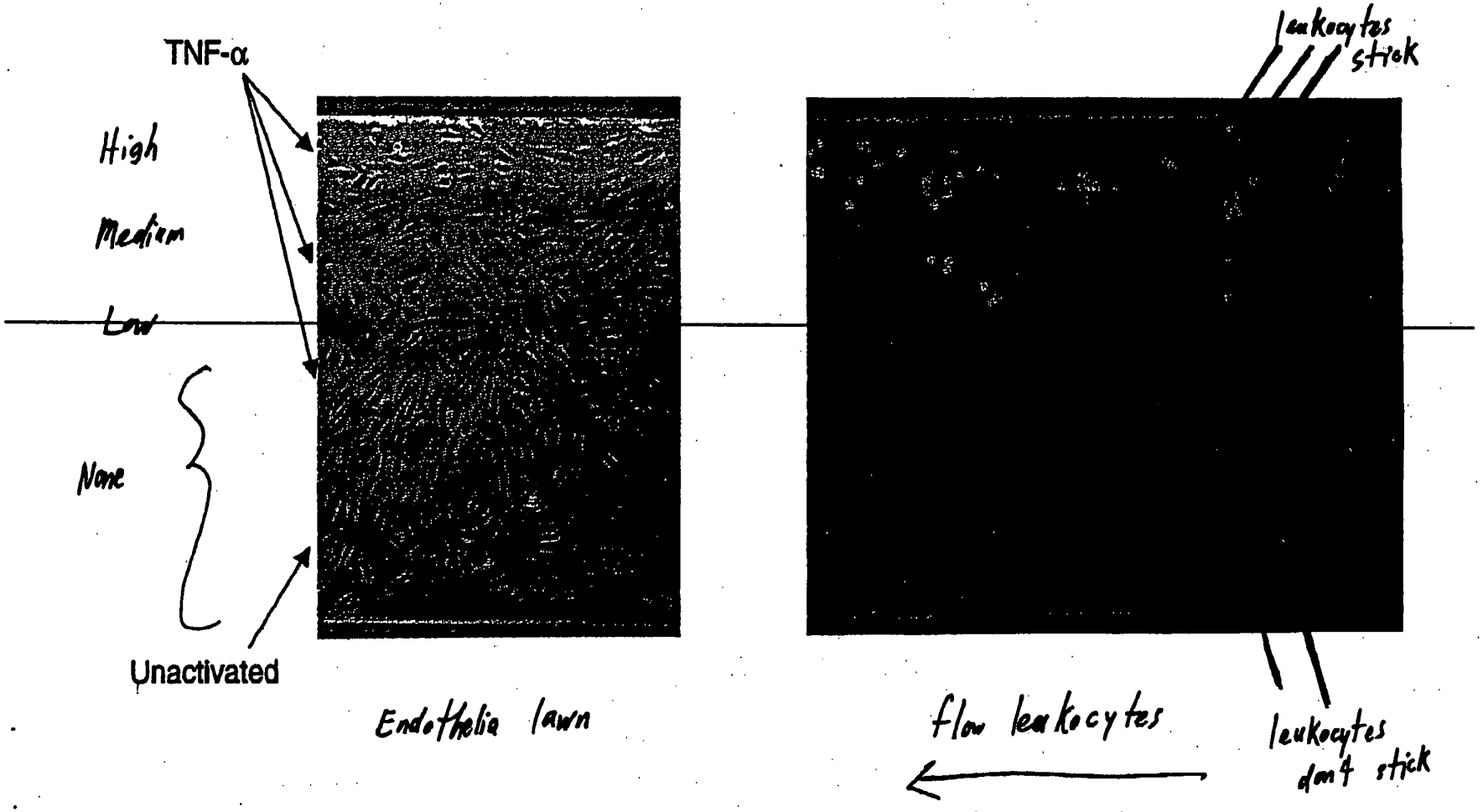


FIG. 85

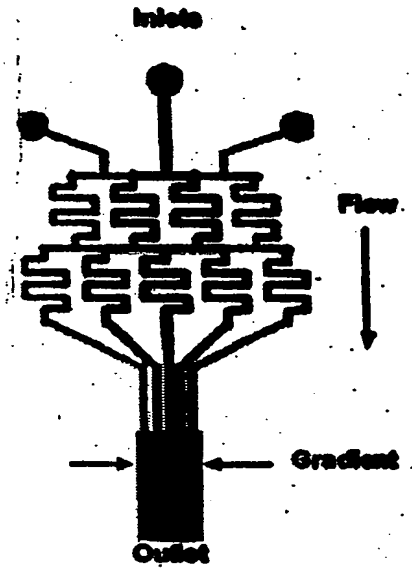


FIG. 86

Strategy and Opportunities

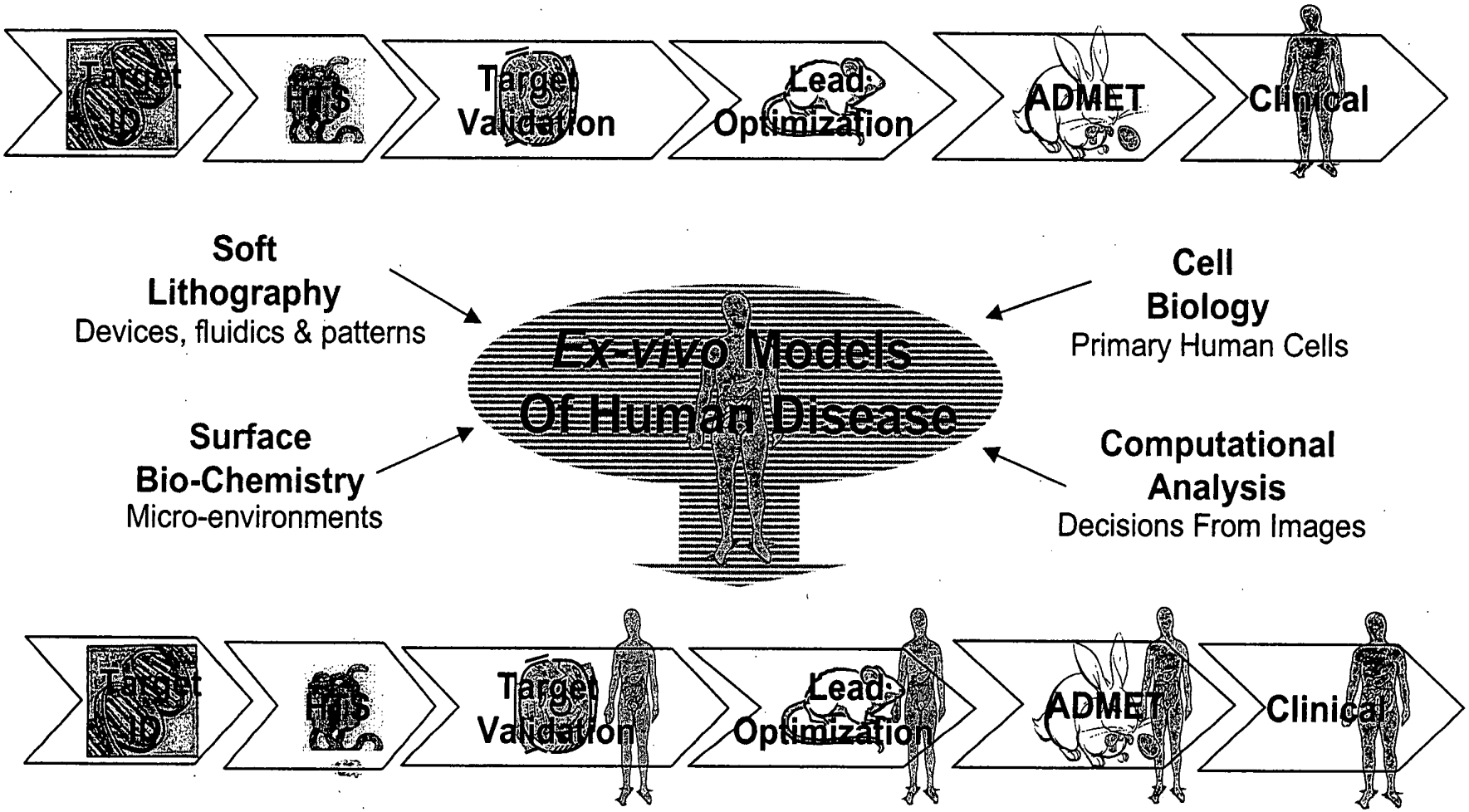


FIG. 87

Creating Subject Profiles

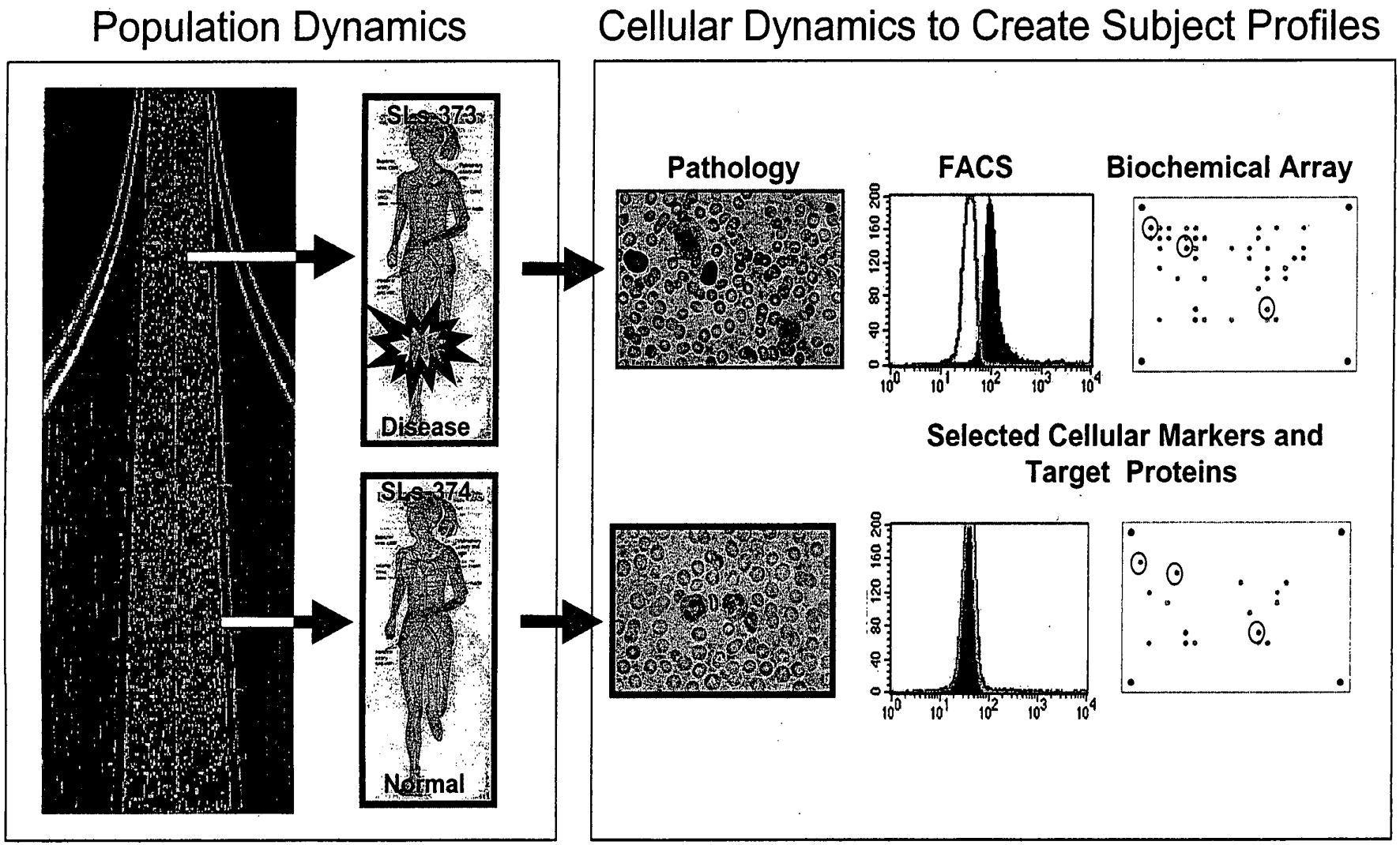


FIG. 88

Pharmacological Response

Subject Profiles

	SLs-373	
FACS	PBMCs	Monocytes
CD14	64%	89%
CD11b (MAC-1)	86%	93%
CD62L (L-selectin)	90%	89%
Target 1	39%	40%
Target 2	75%	92%
Target 3	2%	1%
Target 4	6%	6%

	SLs-374	
FACS	PBMCs	Monocytes
CD14	64%	89%
CD11b (MAC-1)	86%	93%
CD62L (L-selectin)	90%	89%
Target 1	37%	44%
Target 2	5%	8%
Target 3	1%	1%
Target 4	3%	7%

Pharmacological Response

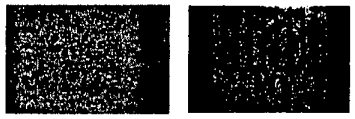
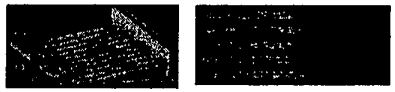
Inflammation- Target 2		
Cellular Events	SLs-373	SLs374
 Activation	SLx 001--XXXX SLx 002--XXXX SLx 003--XXXX SLx 004--XXXX SLx 005--XXXX	SLx 001--XXXX SLx 002--XXXX SLx 003--XXXX SLx 004--XXXX SLx 005--XXXX
 Rolling and Adhesion	SLx 001--XXXX SLx 002--XXXX SLx 003--XXXX SLx 004--XXXX SLx 005--XXXX	SLx 001--XXXX SLx 002--XXXX SLx 003--XXXX SLx 004--XXXX SLx 005--XXXX
 Transmigration	SLx 001--XXXX SLx 002--XXXX SLx 003--XXXX SLx 004--XXXX SLx 005--XXXX	SLx 001--XXXX SLx 002--XXXX SLx 003--XXXX SLx 004--XXXX SLx 005--XXXX
 Chemotaxsis	SLx 001--XXXX SLx 002--XXXX SLx 003--XXXX SLx 004--XXXX SLx 005--XXXX	SLx 001--XXXX SLx 002--XXXX SLx 003--XXXX SLx 004--XXXX SLx 005--XXXX

FIG. 89

Linking Target Expression to Compound Activity- Preclinical

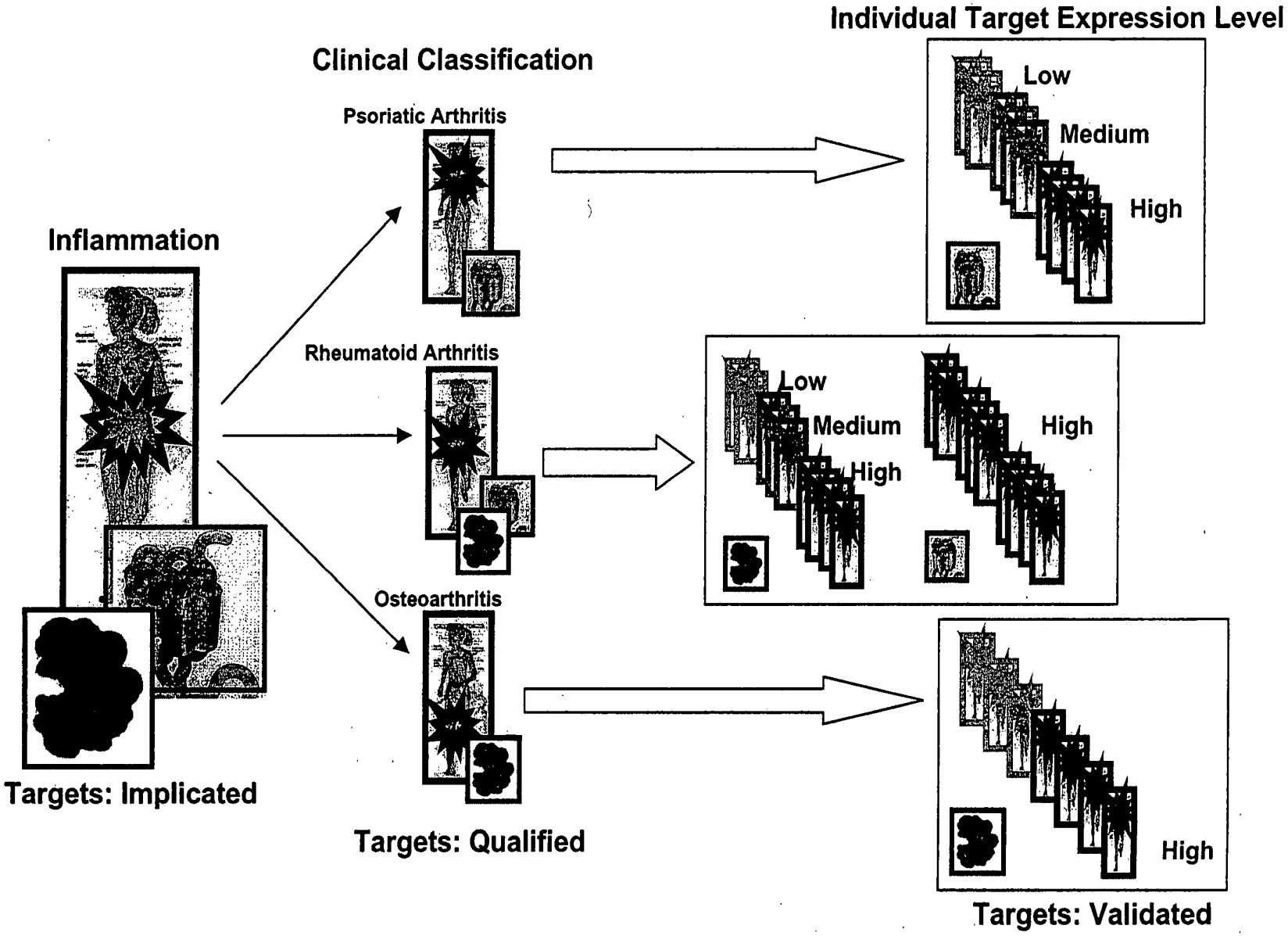


FIG. 90

Linking Compound Activity to Subject Profile-Preclinical

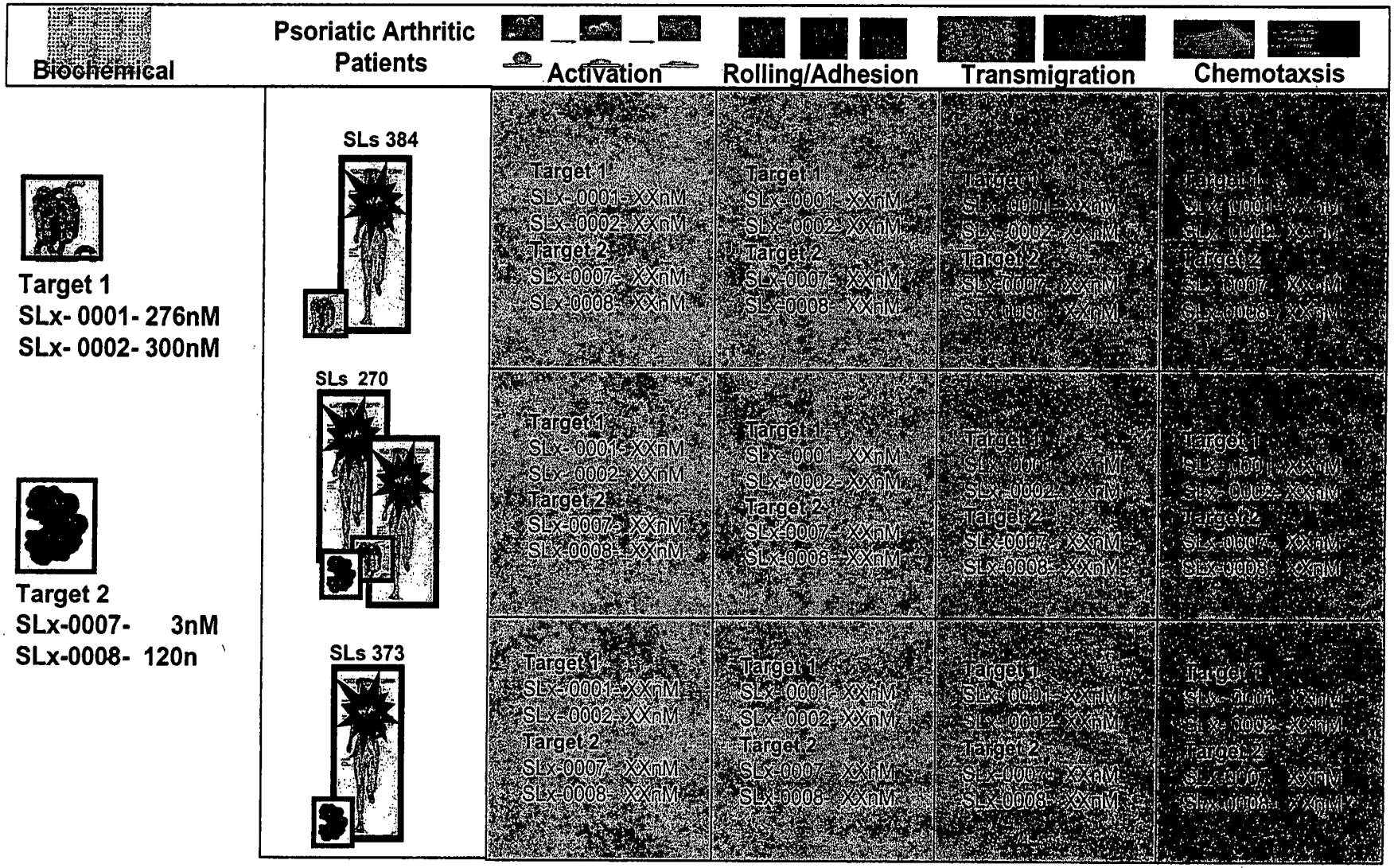
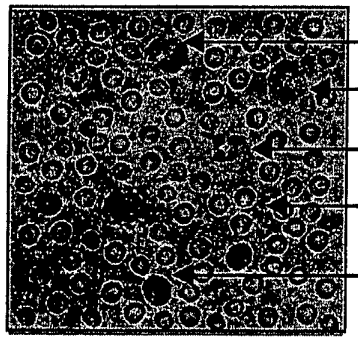


FIG. 91

Targeting Inflammation Disease:
White Blood Cells

Isolation (Control Subjects): **Average Cell Yield Per Unit**



Eosinophil	7M to 10M
Monocyte	25M to 30M
Neutrophil	100M to 200M
Lymphocyte	50M to 80M (CD4+ T cells)
Basophil	<7M

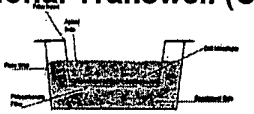
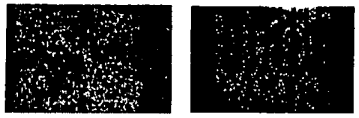
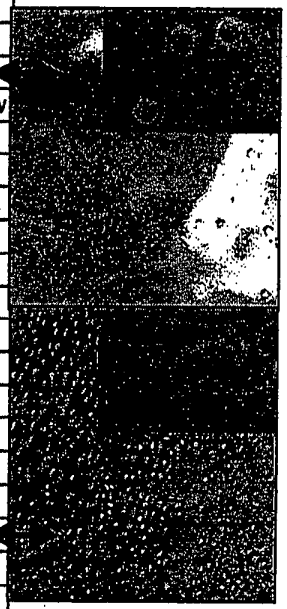
Monocyte Utilization	**Average DATA Points Per Unit**	**Signal to Noise**
Traditional Transwell (Corning)  **Cells Per Well: 500,000 to 1M**	60 total pt 6pt- Total/Blanks 54pt- **3 x 6pt.** IC50 in triplicate	5 to 1
SLx Diapedsis Assay  **Cells Per Unit: 25,000 to 50K**	1,200 pt 20pt- Total/Blanks 1,080pt- **60 x 6pt.** IC50 in triplicate	15 to 1

FIG. 92

Creating a Control Environment

Monocyte Surface Treatments

	Surface	Contact Angle	Adhesion	Activation
Hydrophobic	SLX-C03	102.15	Med	Med
	SLX-C05	114.8	Med	Med
	SLX-C10	89.25	Med	Low
	SLX-C34	103.15	Med	Med
	SLX-C28	111.25	Low	Low
	SLX-C29	90.15	Low	None/Low
	SLX-C26	93	Med	Med
	SLX-C12	97.7	Med	Med
	SLX-C18	84.45	Med	High
	SLX-C25	73.4	High	High
	SLX-C11	77.1	Med	Med
	SLX-C06	78.6	High	High
	SLX-C21	78.4	High	High
Intermediate	SLX-C22	67.4	High	High
	SLX-C30	67.5	Low	Med
	SLX-C01	65.25	High	High
	SLX-C27	61.15	Med	High
	SLX-C24	60.95	Med	High
	SLX-C07	47.7	High	High
	SLX-C20	52.5	High	Med
Hydrophilic	SLX-C02	32.05	Med	Med
	SLX-C23	17.5	Med	Low
	SLX-C19	n/d	Med	High
	SLX-C13	n/d	Med	Med
	SLX-C14	n/d	Med	High
	Glass	n/a	High	High
	TC	n/a	High	High



Monocyte ECM Treatments

SLxG#	Primary Cells and Cell Lines					
	PMN	*Monocyte*	*T-cell*	*Eosinophil*	*THP-1*	*Jurkat*
SLxG110	✗	✗	✗		✓	✗
SLxG111	✓	✗	✗	✗	✓	✗
SLxG112	✓	✓	✗	✗	✓	✗
SLxG113			✗			
SLxG114		✓	✗		✓	
SLxG115		✓	✗		✓	
SLxG116						
SLxG117					✗	
SLxG118	✓	✗	✓		✗	✓
SLxG119	✓	✗	✓		✗	
SLxG120	✓	✗	✓	✓	✗	
SLxG121					✗	
SLxG122					✗	
SLxG123					✗	✗
SLxG124	✓	✓				
SLxG125	✓	✓				
SLxG126						
SLxG127						
SLxG128						✗
SLxG129						✓
SLxG130					✗	
SLxG131					✗	
SLxG132						✓
SLxG133						✗
SLxG134						✗
SLxG135						✗

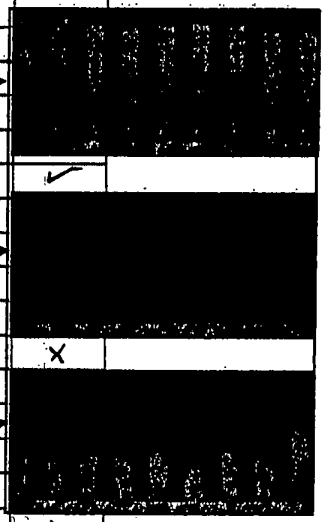


FIG. 93

Targeting Inflammation Disease: Endothelial Cells

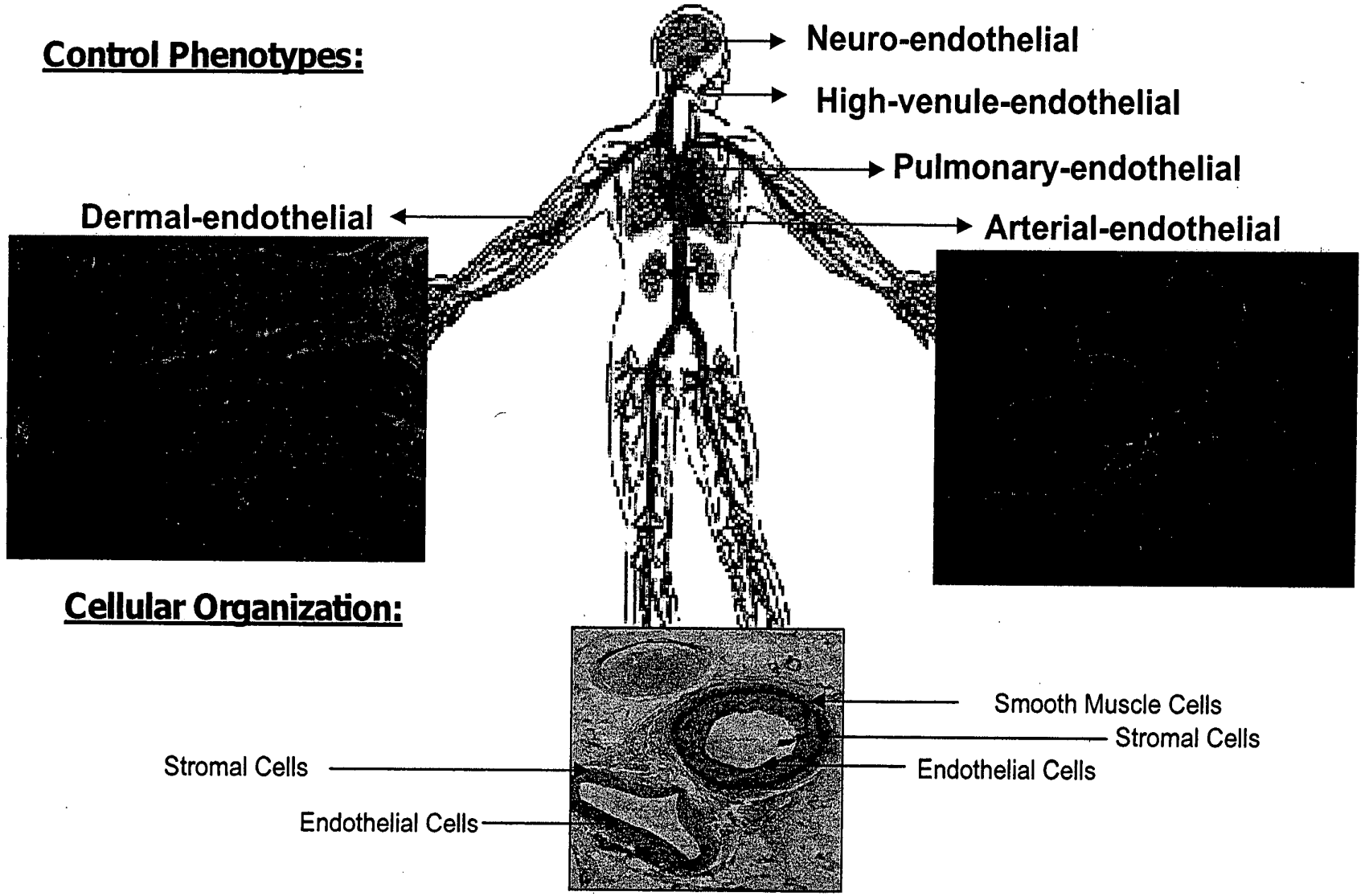
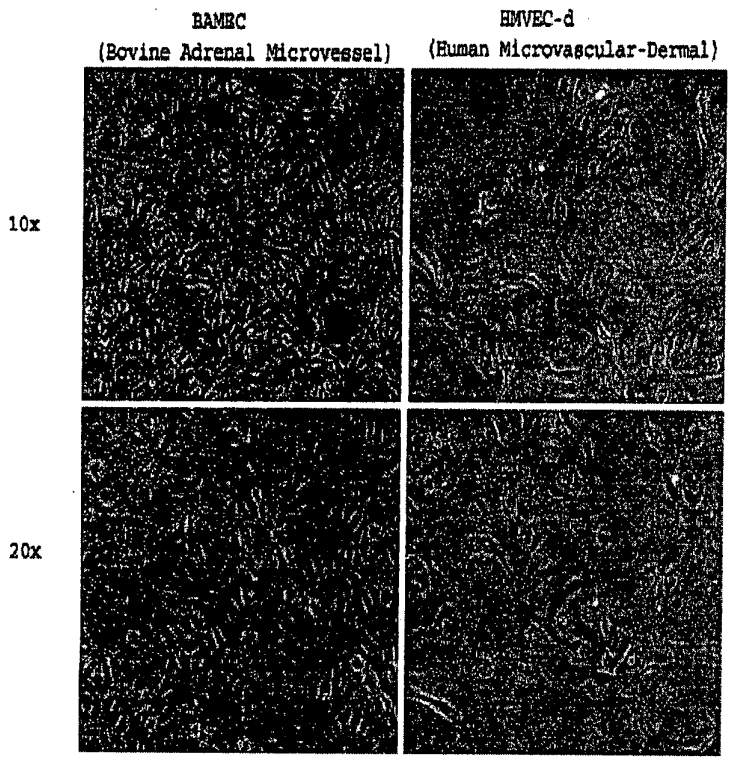


FIG. 94

Creating Capillary Like Structures

Traditional Cell Culture



SLx Cell Culture

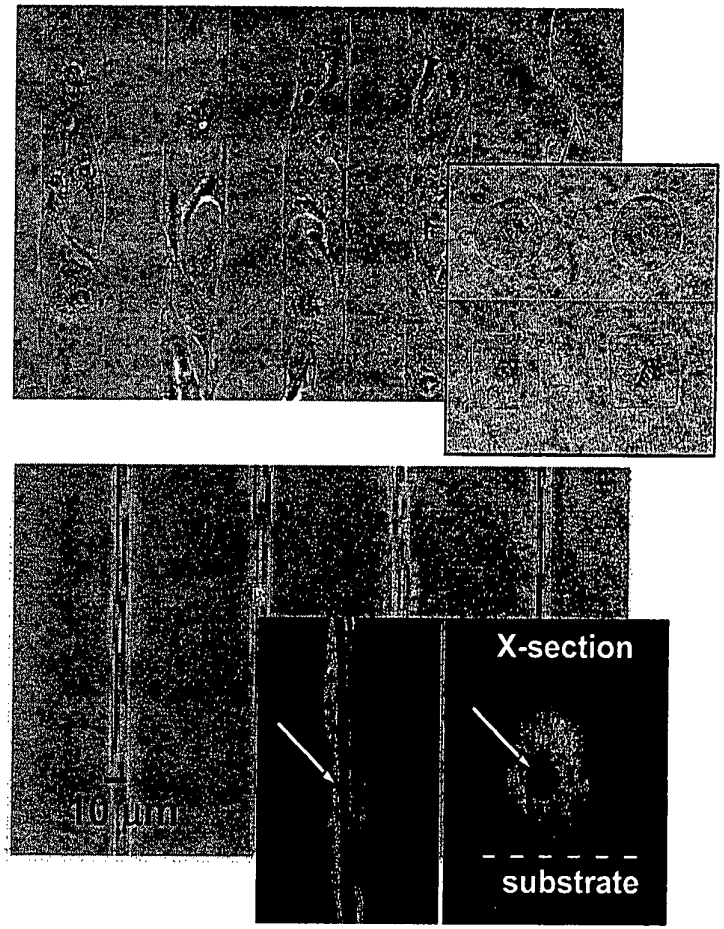
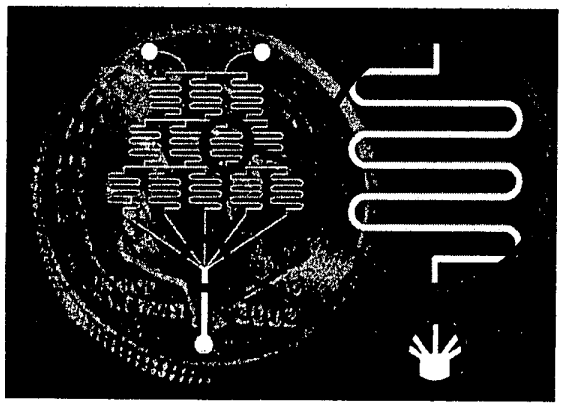
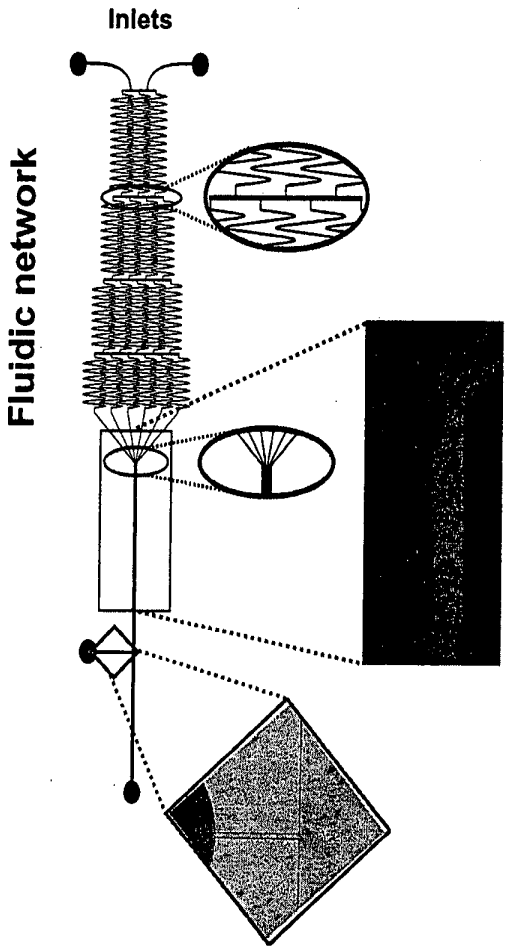


FIG. 95

Targeting Vascular Disease:
Modeling Blood Flow (Gradients/Shear)





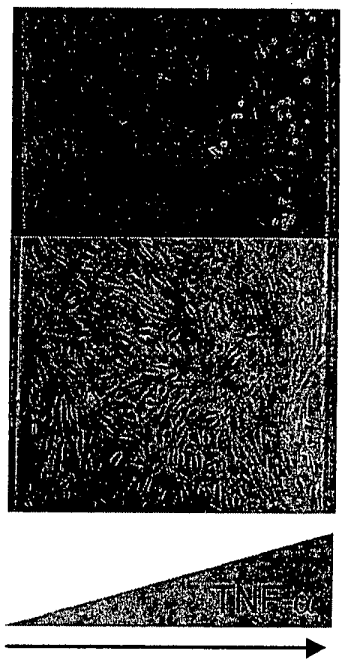
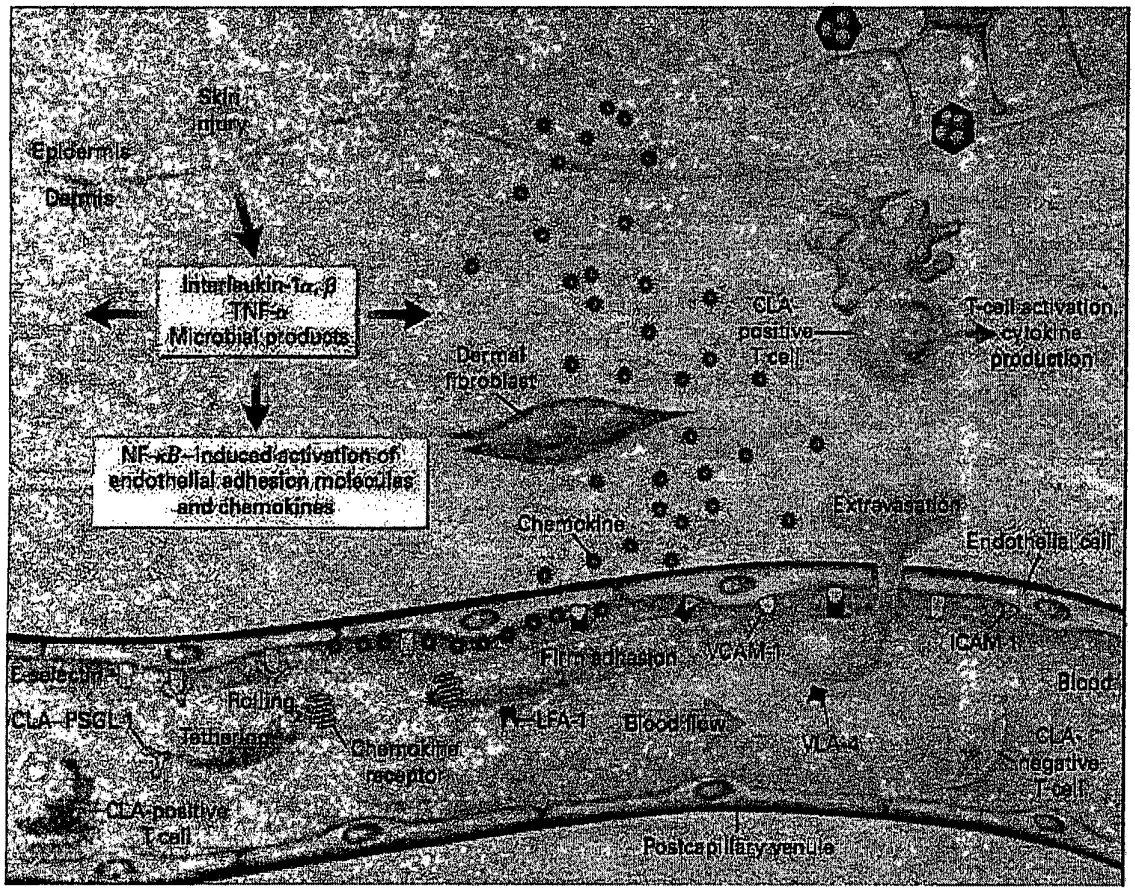


FIG. 96

Inflammation Model

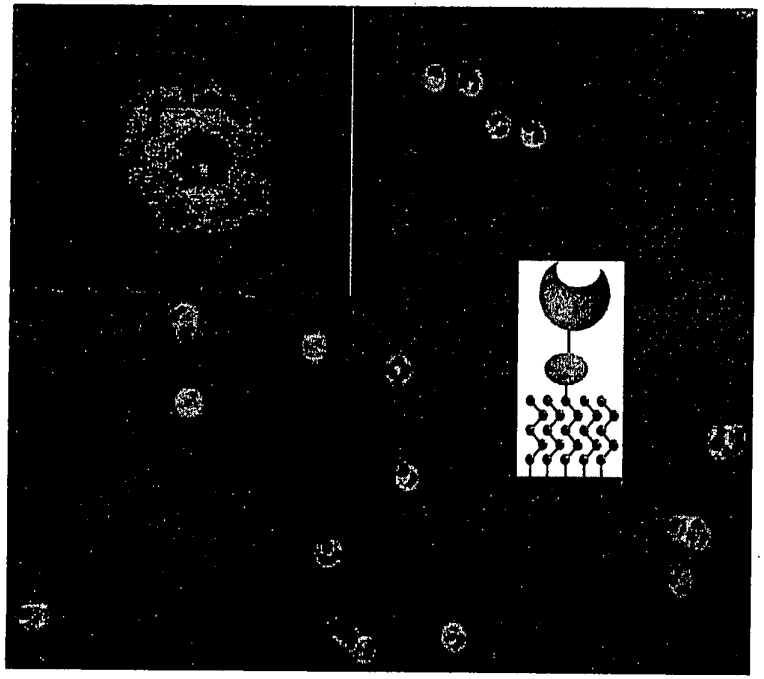


Assays

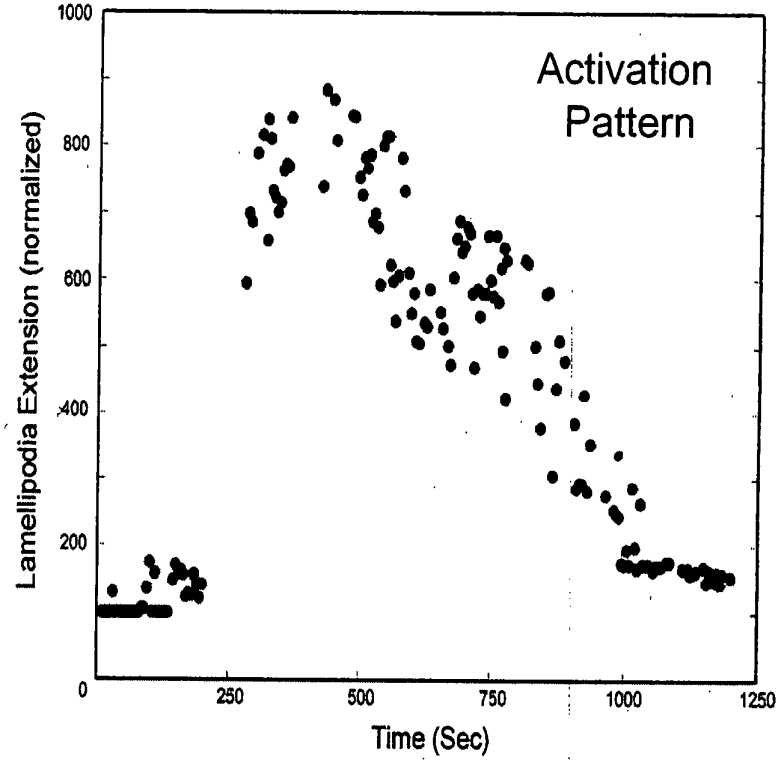
- Target biochemical characterization
- Endothelial cell activation
- Adhesion and Rolling of Leukocytes
- Transmigration of Leukocytes
- Chemotaxis of Leukocytes
- Immobilized Chemokine activation of Leukocyte
- Cell Motility

FIG. 97

Monocyte Activation- Morphology



Lamellipodia Extension
Time Lapse Video



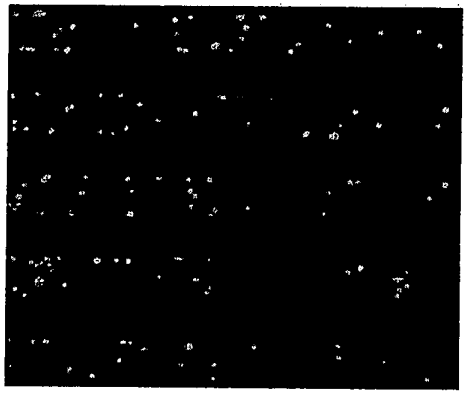
Immobilized Chemokine

FIG. 98

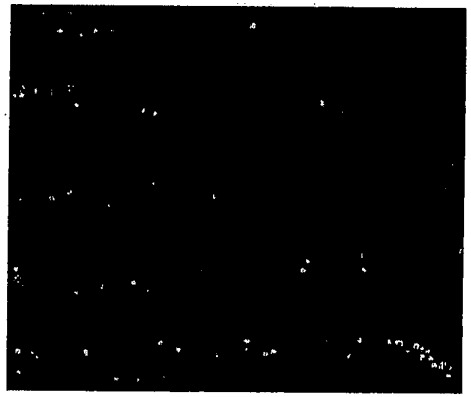
Leukocyte Rolling and Adhesion on Endothelium

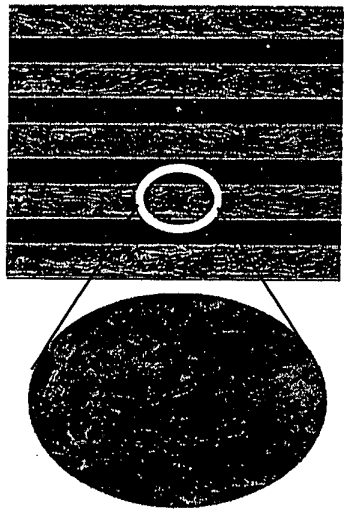
Control: unactivated

Leukocytes on endothelium activated by cytokine



Leukocytes with antibody blocking adhesion





Confluent Endothelial Monolayer

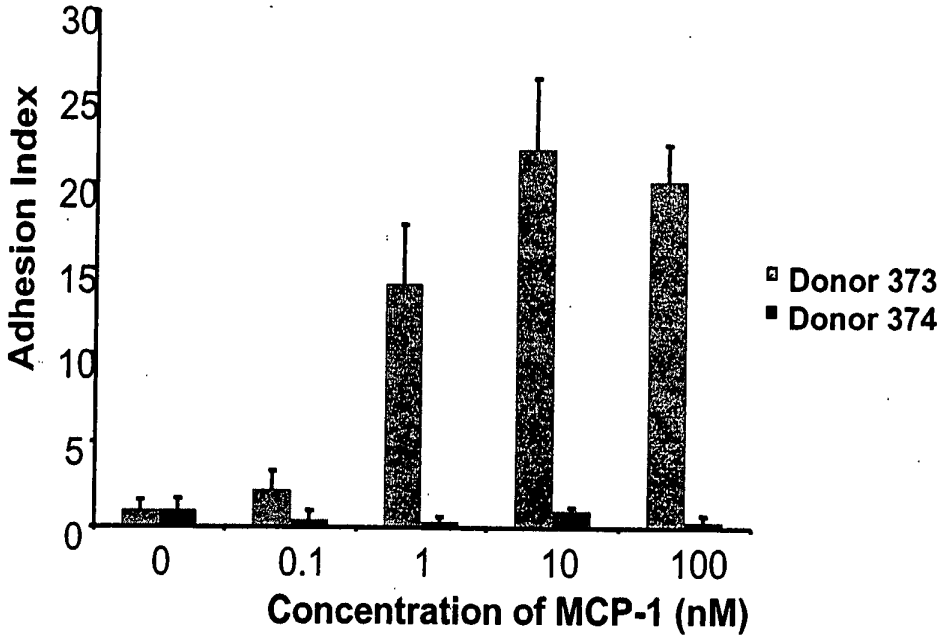
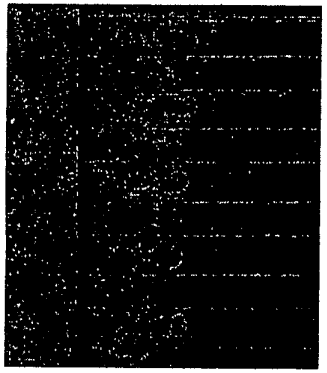


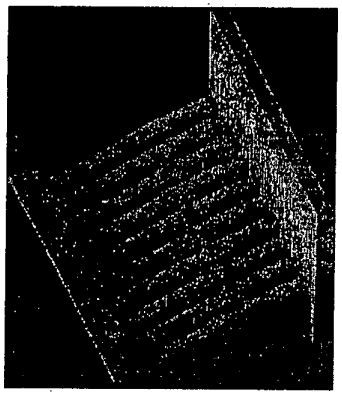
FIG. 99

Chemotaxis of Primary Monocytes

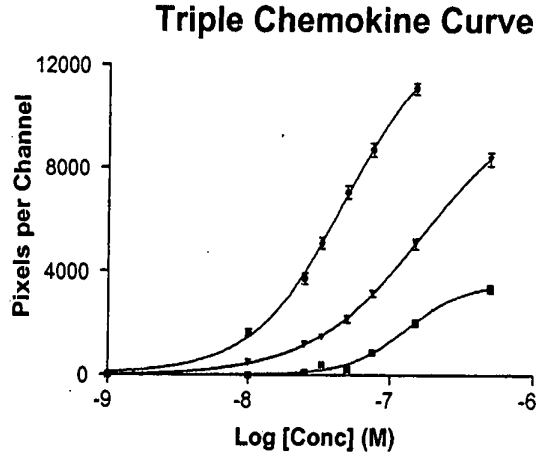
Morphological characterization (with chemokine gradients)



Spatial and temporal readouts



Controlled matrix and stable gradient



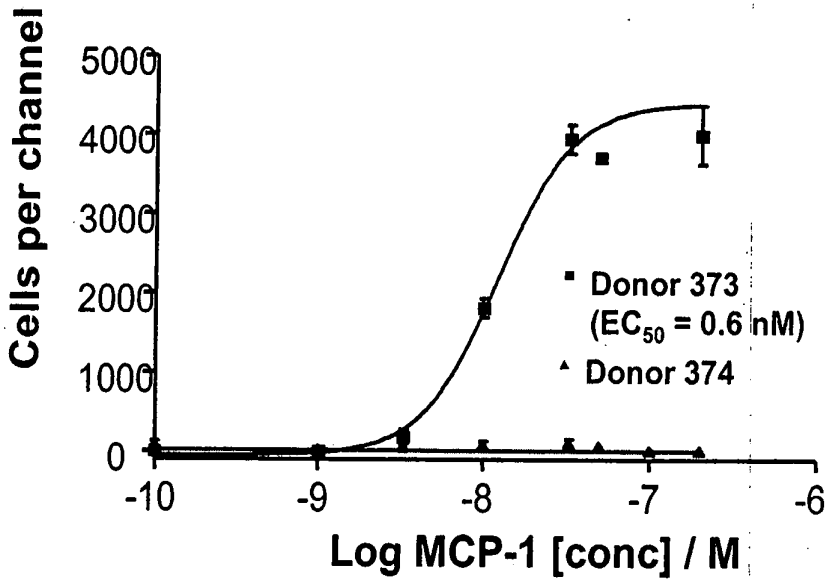
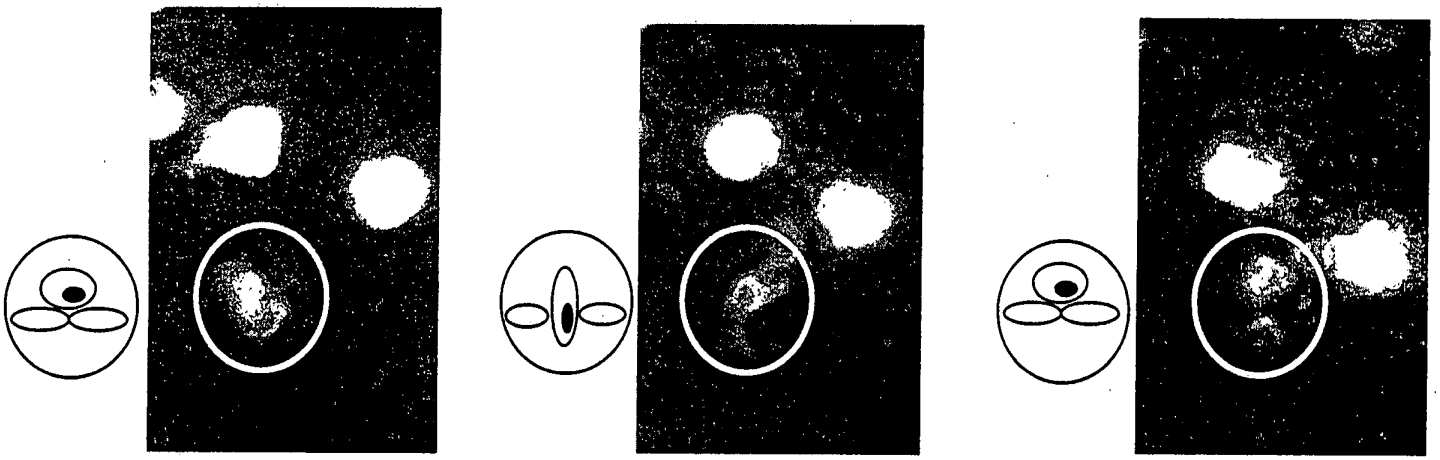
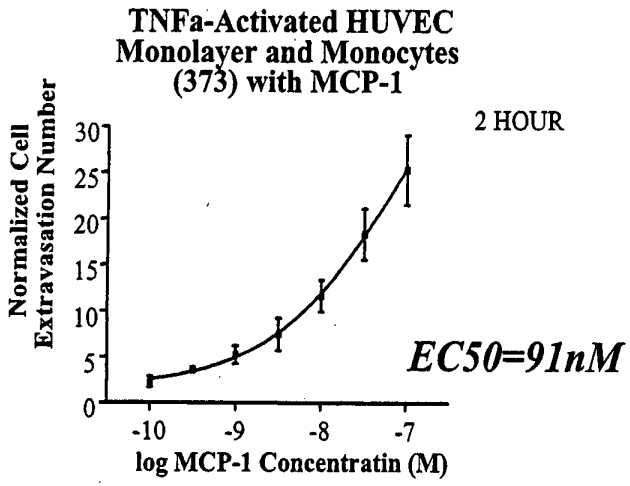


FIG. 100

Diapedesis- Monocytes (SLs 373 & 374)





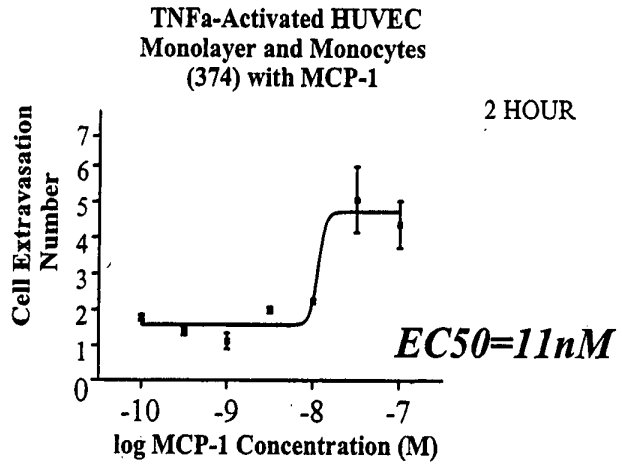
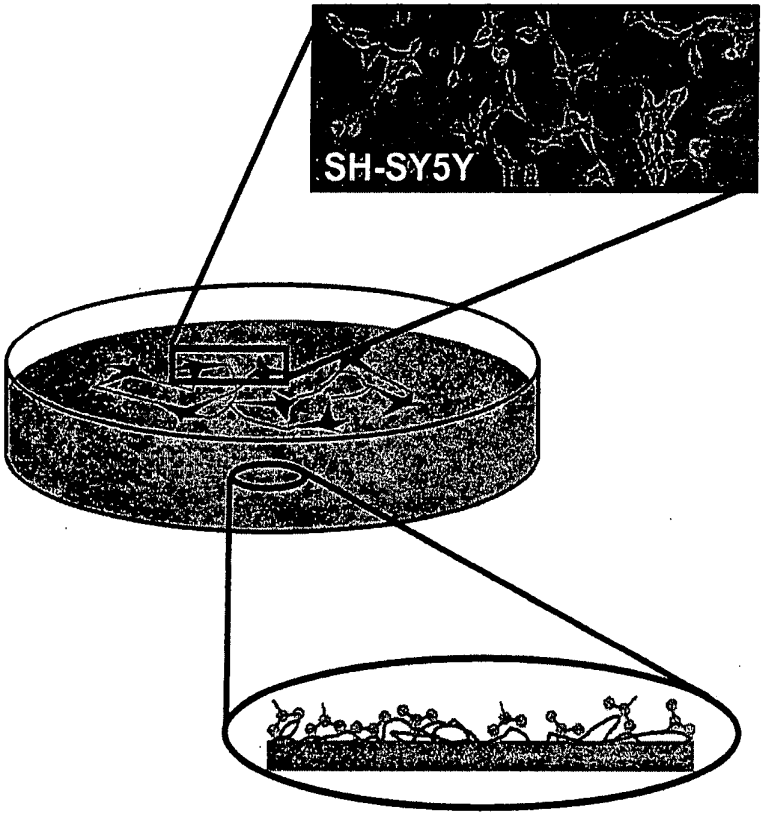


FIG. 101

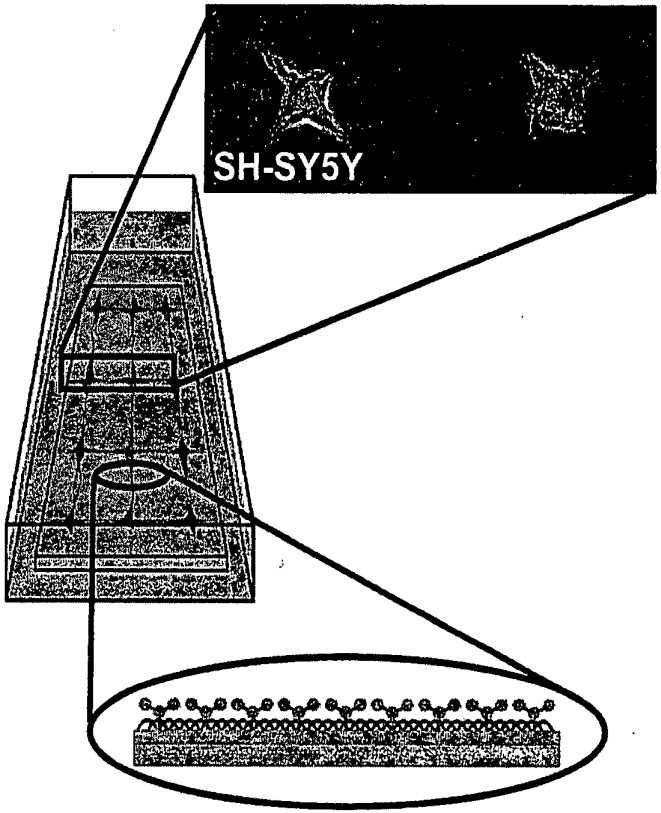
Other Disease Models: Controlled Microenvironments for Complex Cell Cultures

Conventional cell culture



- tissue culture dish
- media
- growth factor

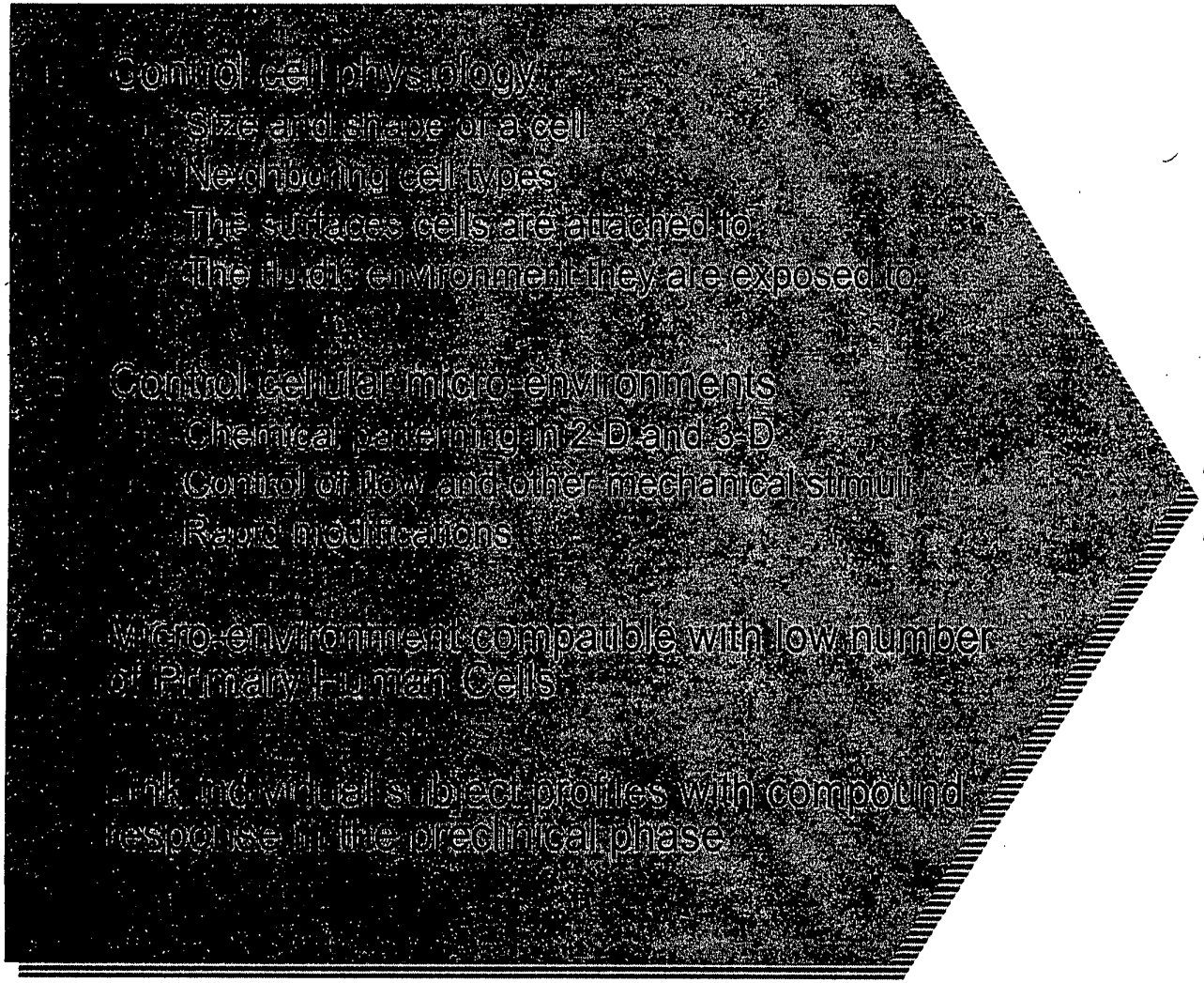
SLx' approach to cell culture



- highly organized ECM-like surfaces
  - fibronectin, laminin, tenascin, collagen, GAGs...
- biological media
- fluidic delivery of growth factors
- predictable connectivity / architecture
- co-culture systems

FIG. 102

Summary



Ex-vivo Models of Human Disease™

FIG. 103